A.M.A. Archives OF

NEUROLOGY AND PSYCHIATRY

SEPTEMBER 1956

VOLUME 76 NUMBER 3

AMERICAN MEDICAL ASSOCIATION Publication

COLONIAL HALL

One of Fourteen units in "Cottage Plan"

For Nervous Disorders

Maintaining the highest standards since 1884, the Milwaukee Sanitarium Foundation continues to stand for all that is best in the contemporary care and treatment of nervous disorders.

Photographs and particulars sent on request.

Josef A. Kindwall, M.D.
Carroll W. Osgood, M.D.
William T. Kradwell, M.D.
Benjamin A. Ruskin, M.D.
Lewis Danziger, M.D.
James A. Alston, M.D.
Edward C. Schmidt, M.D.
Isaac J. Sarfatty, M.D.

★

Waldo W. Buss, Executive Director

Chicago Office—1509 Marshall Field Annex Bldg.
25 East Washington St.—Wednesday, 1-3 P.M.
Phone—Central 6-1162

MILWAUKEE SANITARIUM FOUNDATION, INC.

Wauwatosa Wisconsin

TABLE OF CONTENTS

VOLUME 76 SEPTEMBER 1956 NUMBER 3

SECTION ON NEUROLOGY

ORIGINAL ARTICLES

CORRESPONDENCE

SOCIETY TRANSACTIONS

REGULAR DEPARTMENTS

SECTION ON PSYCHIATRY

ORIGINAL ARTICLES

REGULAR DEPARTMENTS

A. M. A.
Archives of Neurology and Psychiatry

VOLUME 76 SEPTEMBER 1956 NUMBER 3

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee. Change of Address: Notice to the circulation office should state whether or not change is permanent and should include the old address. Six weeks' notice is required to effect a change of address. Second-class mail privileges authorized at Nashville, Tenn., Aug. 6, 1956.

Instructions to Contributors

Communications regarding editorial management, subscriptions, reprints, etc., should be addressed to Specialty Journals, American Medical Association, 535 North Dearborn Street, Chicago 10.

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor of the Specialty Journal concerned. Articles are accepted for publication on condition that they are contributed solely to that journal.

An original typescript of an article should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. A carbon copy should be retained by the author. An article in English by a foreign author should be accompanied by a draft in the author's mother tongue. Improvised abbreviations should be avoided.

The main title of an article may not contain more than seventy characters and spaces; a subtitle may be of any length. The subtitle should be sufficiently detached from the main title that a punctuation mark as strong as a colon can be used in the Table of Contents to separate it from the main title; it must not begin with "with."

The author's name should be accompanied by the highest academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

A Case Report must be preceded by an introductory paragraph containing at least thirty words before the details of the case are given. To avert the possibility of legal action, patients' initials and hospital case numbers should not be published.

Material quoted from another publication must be quoted exactly if the original is in English—spelling, capitalization, punctuation, etc., unchanged. Material taken largely from another publication must be credited to the original author, whether quoted exactly or merely abstracted.

Each article should be accompanied by a summary in the present tense, presenting the main points of the article, but in somewhat more generalized terms than in the article itself.

If it is necessary to publish a recognizable photograph of a person, the photograph must be accompanied by written permission of the subject himself if an adult, or of the parents or guardian if a child, to publish his photograph. An illustration which has been published in another publication must be accompanied by written permission from the author and the original publisher to reproduce it in an A. M. A. Specialty Journal.

The maximum illustration allowance is ten illustrations within a total of 100 sq. inches or $100, whichever is of greater advantage to the author. When no restrictions are placed by the author upon cropping, reducing, and grouping, the publisher is often able to use twenty or more illustrations in one article with the $100 allowance. See an issue of this journal for examples. Oversized originals should be photographed and a print submitted. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author.

Any cut-off marks should be made on the margins (or mountings) rather than on the illustration itself. Charts and drawings should be in black ink on hard, white paper. Lettering must be large enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, an abbreviated title of the article, and top plainly indicated. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be numbered in the order in which they are referred to in the text or listed in alphabetical order without numbers. A chronological arrangement, with all entries for a given year alphabetized according to the surname of the first author, may be used if preferred. References should be typed on a special page at end of manuscript. They should conform to the style of the Quarterly Cumulative Index Medicus, and must include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. Names of periodicals should be given in full or abbreviated exactly as in the Quarterly Cumulative Index Medicus. Reference to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication. Titles of foreign articles, if originally in a generally known Romance or Germanic tongue, must either all be in English translation or all be in the original language. Titles in other languages must be translated. The author must assume responsibility for the accuracy of foreign titles.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

INDEX TO

NEUROPSYCHIATRIC INSTITUTIONS SPECIAL SCHOOLS and SANITARIA Advertising in A.M.A. Archives of NEUROLOGY and PSYCHIATRY

Display announcements of the following institutions appear regularly in A. M. A. Archives of NEUROLOGY and PSYCHIATRY. For advertisements of those institutions which run on an every-other month basis it would be necessary to consult the advertising section of a previous or *subsequent issue*.

when the patient's anxiety is complicated by depression . . .

both symptoms often respond to

THORA-DEX*

(a combination of Thorazine† and Dexedrine‡)

'Thora-Dex' is a combination of a specific anti-anxiety agent, 'Thorazine', and a standard antidepressant, 'Dexedrine'. The preparation is of unusual value in mental and emotional disturbances and in somatic conditions complicated by emotional stress—especially when depression occurs together with anxiety, agitation or apprehension.

The patient treated with 'Thora-Dex' is generally both calm and alert . . . with normal interest, activity and capacity for work.

Smith, Kline & French Laboratories, Philadelphia

'Thora-Dex' Tablets are available in two strengths:

10 mg. 'Thorazine'	25 mg. 'Thorazine'
2 mg. 'Dexedrine'	5 mg. 'Dexedrine'

'Thora-Dex' should be administered discriminately and, before prescribing, the physician should be fully conversant with the available literature.

*Trademark †T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

‡T.M. Reg. U.S. Pat. Off. for dextro-amphetamine sulfate, S.K.F.

THE MILTOWN MOLECULE

A tranquilizer well suited for prolonged therapy

NO ORGANIC CONTRAINDICATIONS

reported to date

- well tolerated, non-addictive, essentially non-toxic
- no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness
- chemically unrelated to chlorpromazine or reserpine
- does not produce significant depression
- orally effective within 30 minutes for a period of 6 hours

Indications: anxiety and tension states, muscle spasm.

Miltown®

the original meprobamate—2-methyl-2-n-propyl-1,3-propanediol dicarbamate—U.S. Patent 2,724,720

SUPPLIED: 400 mg. scored tablets. Usual dose: 1 or 2 tablets t.i.d.

DISCOVERED AND INTRODUCED by Wallace Laboratories, New Brunswick, N. J.

Literature and Samples Available on Request

Section on NEUROLOGY

Infantile Encephalomalacia with Multiple Cavity Formation

BERNARD J. ALPERS, M.D.
RODNEY A. FARMER, M.D.
and
H. EDWARD YASKIN, M.D., Philadelphia

Sporadic reports of encephalomalacia with cavity formation in infants have appeared in the literature. An increasing number of such reports has appeared in the past several years, and with them has come increasing recognition of the condition as a disease entity. Thus far, much more is known regarding the pathological than the clinical features of the disorder. We report another case tending to elaborate the pathology of the disease.

Report of a Case

Little is known regarding the patient, who was a white boy of 3½ months. The mother was in good health during pregnancy but one week before delivery suffered an attack of pneumonia. The birth history was reported as normal. There were no seizures at birth. At 2 weeks of age the infant developed "growling respirations," and at 7 weeks he had a bloody nasal discharge, extended his arms stiffly, and was noted to have a staring gaze. At 11 weeks he had attacks of cyanosis, in which he was found to twitch, stiffen out, and clench his fists. He had a generalized convulsion at 14 weeks. Examination at this time revealed that the child was unconscious, with hyperpnea, bilateral papilledema, retinal and subhyaloid hemorrhages, and generalized hyporeflexia. The spinal fluid and subdural fluid were grossly bloody. He had an erythrocyte count of 2,700,000 and 41,000 leucocytes per cubic millimeter, with lymphocytes predominating. He died within a few hours after his seizure.

Received for publication April 3, 1956.

From the Department of Neurology, Jefferson Medical College of Philadelphia.

Apart from fetal lobulation of the kidneys, hypoplasia of the adrenals, and generalized visceral congestion, the general autopsy revealed nothing abnormal.

Gross Brain.—The brain measured 15×12×6 cm. and weighed 670 gm. The brain was small and atrophic. The pia-arachnoid membranes were clear but stripped with difficulty and revealed a friable cortex. The blood vessels of the circle of Willis appeared normal. Over the left frontal pole, the frontal and parietal lobes near the midline, and the left occipital lobe were areas of recent subarachnoid hemorrhage. The base of the brain was covered with a thin film of subarachnoid hemorrhage, sufficient to obscure the underlying structures. Near the right Sylvian fissure was a shrunken, distorted area (2×3 cm.), which was firm and hard. Small, firm areas were felt in both occipital lobes. At the right parieto-occipital junction a small, fluctuant cyst was grossly visible.

Coronal sections of the brain revealed pallor of the centrum semiovale. There were numerous cystic areas throughout the gray matter of the cortex and in the subcortical areas, and in the basal ganglia regions, producing a beehive appearance of the involved areas. Larger cysts were seen near the surface and were at times multiloculated. None of them had a ventricular connection. The cortex was more severely destroyed in most areas than was the white matter. The brain stem and cerebellum were not involved. The spinal cord was not available for study.

Microscopic Examination.—There were areas of softening throughout the tissue, characterized by a reduction in the number of ganglion cells and by large collections of gitter cells, sharply defined from the adjacent tissue.

The pia-arachnoid was thickened in many areas, particularly over the affected cortex (Fig. 1).

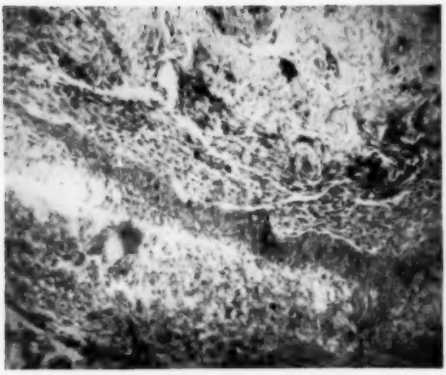


Fig. 1.—Thickened, fibrous pia-arachnoid containing macrophages of various sorts, overlying a part of the cerebral cortex. Toluidine blue stain.

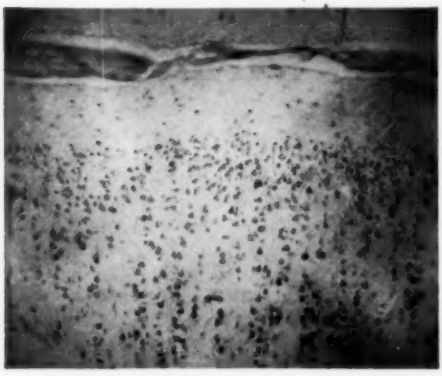


Fig. 2.—View of the upper layers of cerebral cortex, showing loss of ganglion cells and eroded areas. Toluidine blue stain.

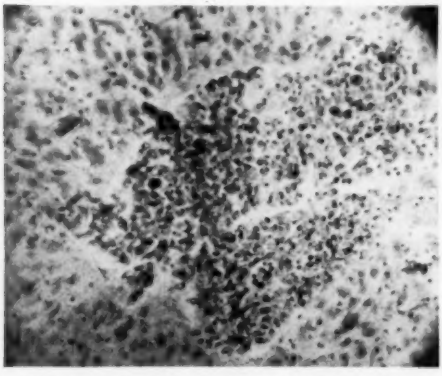


Fig. 3.—Island of gitter cells in the white matter, surrounded by swollen astrocytes. Toluidine blue stain.

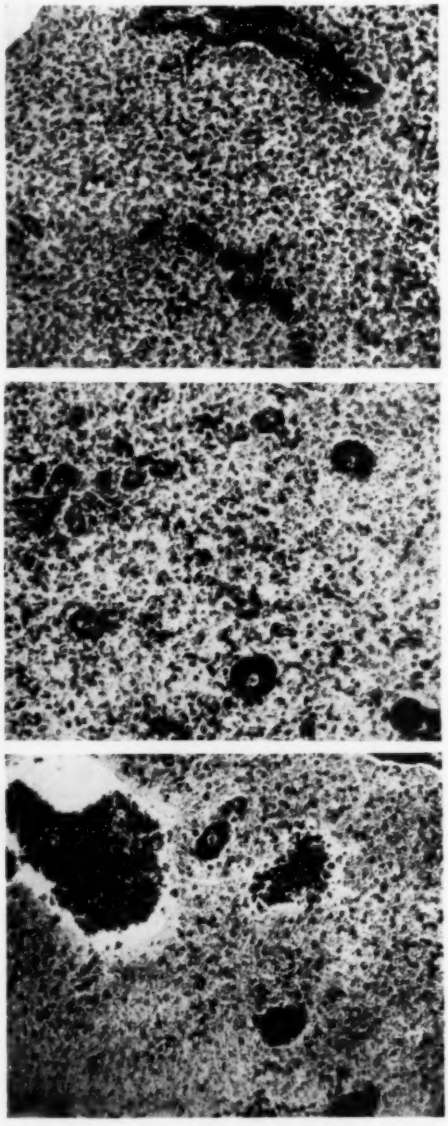


Fig. 4.—(Top) Fat stain, showing a large area of softening in the cortex, with gitter cells packed with fat; scharlach R stain. (Middle) A similar area in the white matter. (Bottom) A similar area, showing the islands in the white matter filled with fat-packed gitter cells.

Fibrosis was present and in some parts was quite marked. The meninges were not adherent. Macrophages were numerous, some of them containing hemosiderin. No leucocytes were seen. In a few areas small collections of red cells were seen over

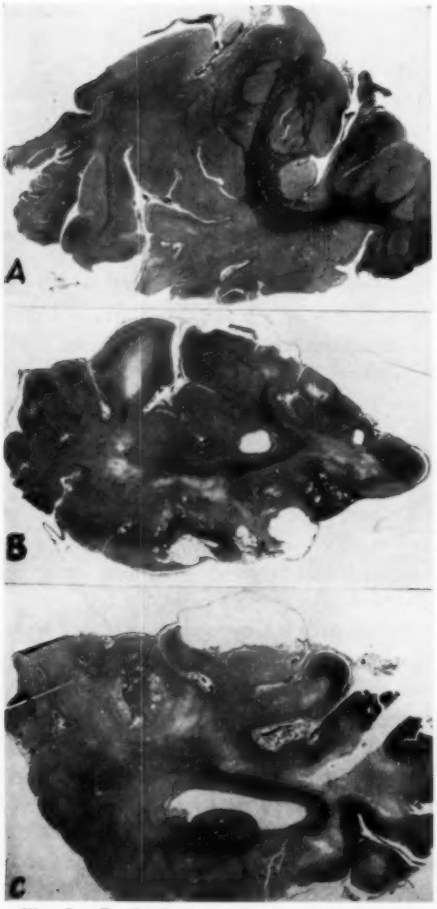


Fig. 5.—Cerebral cortex from temporal and occipital areas, showing failure of myelination. Weil stain.

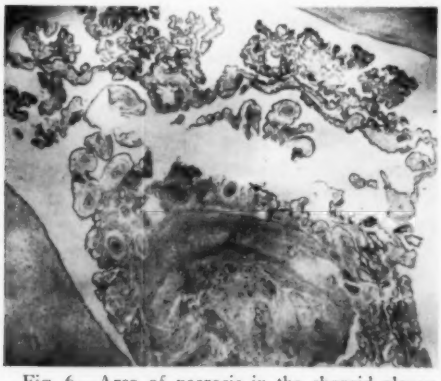


Fig. 6.—Area of necrosis in the choroid plexus. Toluidine blue stain.

the cortex. The blood vessels in the meninges were often dilated, and the walls of the arteries often seemed homogeneous and appeared hyalinized.

The cerebral cortex and underlying white matter were affected by the disease process in many areas, but the entire brain was not affected. All parts of the cerebrum were involved (frontal, temporal, parietal, and occipital), but within the affected regions the cortex was not universally diseased (Fig. 2). The cortex was more severely involved than the white matter, the latter being affected alone or together with the underlying tissue. Three general types of reaction were encountered: (1) areas of complete, or almost complete, cortical destruction; (2) areas of incomplete destruction, and (3) areas of focal destruction.

Within the areas of complete destruction few or no nerve cells were seen. When present, they were found to be swollen and diseased. For the most part the cortex in these regions had been displaced by gitter cells (Fig. 3), in varying numbers, and swollen astrocytes. The latter were seen in profusion not only in the midst of the destroyed areas but around them as well. In some areas the destructive process had gone on to complete destruction with cavity formation. In a few places the cavity was multiloculated. The cavity was lined by a thin film of arachnoidal tissue. Surrounding it were large numbers of plump astrocytes.

In the partially destroyed areas the process was fundamentally the same, except that more nerve cells were present. Fat stains revealed large numbers of fat granules in the gitter cells (Fig. 4). These were sometimes arranged around blood vessels. Plump astrocytes were present in great abundance in some areas, surrounding partially destroyed areas of cortex. The ganglion cells in the partially destroyed regions varied in appearance. The Nissl substance was often absent or pulverized. The cytoplasm was swollen in many instances; in others the cells were shrunken. Myelin-sheath stains revealed incomplete myelin deposit in all parts of the cortex and demonstrated clearly the tendency to cavity formation (Fig. 5).

In some areas of the cortex and white matter were what appeared to be focal collections of gitter cells. In their midst could usually be seen a vessel, but this was not always present. An area of necrosis was noted in the choroid plexus (Fig. 6). Deposits of calcium were seen in some of the areas of necrosis both in the cortex and in the white matter. These were extracellular and consisted of discrete calcium granules, as well as larger deposits of calcium. The calcium was found also within the cytoplasm of large cells, but sometimes as a mass within multinucleated cells. Calcification of the smaller blood vessel walls was seen in some areas. Multinucleated

giant cells were often seen scattered throughout the cystic areas.

The blood vessels of the meninges showed slight thickening of the media at times. The intima appeared to be edematous in the small and medium-sized arteries, with swelling of the endothelial cells in many arterioles. In the cortex the arteries showed swelling of the endothelium with almost complete obliteration of the lumen. The endothelial cells of most of the capillaries were swollen and stained poorly. The perivascular spaces of many of the vessels were filled with macrophages and scattered mononuclear cells. In some of the arterioles within the cortex there was proliferation of the endothelial lining, often with two or three layers of endothelial cells, and with narrowing of the vessel lumen. In those areas of the cortex where there was proliferation of astrocytes the capillaries were more prominent, and the arterioles at the margins of such areas showed evidence of hyaline degeneration.

The cortex in general and the brain stem showed evidence of inadequate myelin formation consistent with the age of the patient.

Comment

Infantile encephalomalacia has been recorded in several instances, but the number of recorded cases is not large. With minor differences, the various reports are in general agreement concerning the characteristics of the disorder.

Gross Brain.—The brain is characterized by the presence of cavity formation, the cavities varying in size, location, and number from one specimen to another. The white matter has been more severely affected than the cortex in all cases except in the present case, where the reverse was true. It has been observed, however, that the cortex is not entirely spared in some instances (Stevenson and McGowan,[1] Lumsden[2]). The cortex has been described as looking and feeling gelatinous (Winkelman and Moore[3]) and as leathery (Marburg and Casamajor[4]). The cortical gyri have been described as small (Winkelman and Moore), atrophic (Marburg and Casamajor), soft and shrunken (Ford[5]), shrunken (Lumsden), and as having marked generalized microgyria (Negrin, Lepow, and Miller[6]). The cerebellum is not usually affected by the process but has been described as having a gelatinous appearance (Winkelman and Moore; Negrin, Lepow, and Miller), and in one instance large lesions were found in the lateral hemispheres of the cerebellum (Ford). No cavities are found in the brain stem, basal ganglia, or spinal cord (Ford), while the examination of the gross brain reveals nothing significant as a rule in the basal ganglia or cerebellum; necrotic areas have been found in the former (Winkelman and Moore; Stevenson and McGowan). Areas of demyelination have been described in the cerebellum, on microscopic study (Winkelman and Moore), and thinning of the myelin in the cerebellar leaflets (Stevenson and McGowan).

In one of the early reported cases the right cerebral hemisphere was atrophied, and cyst-like areas were found in the right frontoparietal region, extending into the occipital lobe, as well as in the left parieto-occipital area (Diamond[7]). Of seven reported cases, all were found with many well-defined cavities in the white matter, associated with varying degrees of hydrocephalus (Stevenson and McGowan). The brain in another instance showed cystic gelatinous degeneration of the greater part of the subcortex of the frontal lobes, with the formation of fairly large cystic cavities, and a large cystic cavity in the left occipital lobe (Winkelman and Moore). Cystic areas were found bilaterally involving "the greater part of the hemispheres" (Marburg and Casamajor); in another instance a large cyst was found in the frontal lobe (Marburg and Casamajor). Multilocular cyst formation extending from the frontal to the occipital pole in both hemispheres and involving the cortex and white matter has been reported (Lumsden), and cavities with fine trabeculations have been observed (Negrin, Lepow, and Miller).

Microscopic Examination.—The several cases which have been recorded revealed evidence of softening or encephalomalacia, with attempts at reparative processes, and with eventual cyst formation. Cysts are

not always found, however (Case 2, Diamond). The over-all picture, therefore, is one of softening with eventual cyst formation, and with indications of transition processes between the two extremes.

The meninges have been found to be thickened, and in the arachnoid are found fibroblasts, polyblasts, lymphocytes, gitter cells, and macrophages (Diamond). Slight fibrosis of the meninges has been observed (Marburg and Casamajor). In another instance the pia-arachnoid was distended, the subarachnoid space containing monocytes, phagocytes, endothelioid cells, and immature granulocytes (Winkelman and Moore). The pia-arachnoid elsewhere has been described as showing a slight generalized thickening and loss of translucency (Lumsden). In the present case the pia-arachnoid was thickened and fibrotic but not adherent to the underlying cortex, and contained numerous macrophages (Alpers, Farmer, and Yaskin).

The affected areas of softening contain gitter cells in varying amounts, reduction in the number of ganglion cells, and evidence of glial proliferation (Diamond), with some foci containing extensive deposit of calcium salts in and among the ganglion cells. In another case the cerebral cortex was for the most part a thin shell, the ganglion cells showing advanced severe cell disease, associated with gitter-cell formation and intensive astrocyte proliferation, with complete symmetrical demyelination of the white matter of the cerebral hemispheres, with enormous amounts of fat in the cortex, and with hypertrophy of the endothelial nuclei of the capillaries (Winkelman and Moore). Necrotic areas were found in the basal ganglia; the Purkinje cells of the cerebellum were swollen, and there were areas of complete demyelination in the cerebellum, but no cyst formation was found. In addition to the gitter cells and astrocytes usually found in the areas of softening, irregular foci of sclerosis have been described, with collections of gitter cells in the walls of some of the cysts (Marburg and Casamajor). Large accumulations of gitter cells have been seen in the perivascular spaces in and around the areas of softening, astrocyte proliferation around the capillaries and venules, large amounts of fat within the gitter cells, and demyelination in the affected areas (Lumsden). The cavities were found to be surrounded by a compact layer of neuroglial fibers, astrocytes, and fat-laden gitter cells; and large deposits of fat were noted in the gray and white matter, including nerve cells, with a few deposits of amorphous calcium. There was almost complete absence of myelin (Negri, Lepow, and Miller).

The blood vessels have been reported to be normal in some instances. In others there have been observed hypertrophied endothelial nuclei of the capillaries (Winkelman and Moore), "signs of endothelial growth" of the arteries in the meninges (Marburg and Casamajor), and thickened blood vessel walls (Diamond). In some instances associated with syphilis there was evidence of periarteritis (Stevenson and McGowan), but in seven cases which they reported Stevenson and McGowan found "no notable change in the arteries in any of the sections examined." The cortical vessels were found to be sclerosed and calcified in the areas of cyst formation (Marburg and Casamajor).

Clinical Observations.—It is difficult to correlate the clinical facts with the pathological observations in the recorded cases, chiefly because the emphasis has been on the brain changes, and partly because, in those instances in which clinical observations have been recorded, there has been little common to all cases. The one outstanding feature of all the reported instances has been their occurrence in infants, varying in age from 15 days (Negrin and associates) to 7 weeks (Diamond, Lumsden), 12 weeks (Winkelman and Moore), 3½ months (Diamond), 9 months (Marburg and Casamajor), 3 years (Marburg and Casamajor), and 3½ months (Alpers, Farmer, and Yaskin). The condition is apt to appear in the first year of

life, but has been recognized up to the age of 3 years.

Labor has usually been normal and at full term, but in one instance the labor was prolonged and resuscitation was difficult. No mention is made of prematurity in the recorded cases, and the presumption is that the patients were born at full term. Seizures were relatively frequent and were recorded in four cases. Convulsive movements (Winkelman and Moore; Marburg and Casamajor) and clonic movements of the left hand and right leg (Lumsden; Negrin, Lepow, and Miller) have been reported. Athetoid movements have been seen (Diamond). Neurological examination has revealed spasticity of all the limbs with a bilateral positive Babinski sign (Winkelman and Moore; Marburg and Casamajor), and optic atrophy (Marburg and Casamajor).

Pathogenesis.—The cause of the condition is unknown. Attempts have been made to correlate the brain changes with occlusion of the vessels. Marburg and Casamajor found occasional thrombi in the cortical veins and on this basis attributed the brain damage to phlebothrombosis and phlebostasis, caused chiefly by trauma before, during or after birth. They stated:

> The site of the lesions corresponds to the drainage area of the veins: the centrum semiovale, the area of the vena terminalis anterior, and the vena lateralis ventriculi of the great vein of Galen (vena cerebri magna); the cortex and the adjacent parts of the meditullium, drained by the sinus longitudinalis superior. The pathologic changes are necrosis, malacia, and serous profusion, followed by total or partial destruction of the tissue, with sparing of the most resistant parts (glia) and destruction of the least resistant structures (myelin sheaths and axons).

Lumsden, on the other hand, found no evidence of thrombosis in his case and regarded the process as degenerative. Winkelman and Moore asserted that "the clinical and pathologic aspects of the condition . . . resemble in most details 'swayback' in lambs." Lumsden agreed that the microscopic features of the disorder resemble those of swayback. He regarded the process as essentially degenerative, as did Ford, and stated that "attention is drawn to the possible role of transsynaptic degeneration and the much greater ferment activity in the production of malacia in degenerative disease of the central nervous system of the infant."

Our studies fail to shed new light on the nature of the disease process. The probabilities favor a degenerative process, the origin of which is not clear from a study of the reported cases. The distribution of the lesions makes it improbable that they are the result of vascular disease. While changes in the blood vessels were found in our case, they were not of sufficient degree to produce encephalomalacia, and in the cases reported disease of the vessels was not always found to be present.

Summary

We report an instance of infantile encephalomalacia in an infant of 3½ months, characterized by numerous cystic areas in both gray and white matter of the brain and in the basal ganglia regions, and sparing brain stem and cerebellum. Microscopic study revealed pia-arachnoid thickening, profuse gitter-cell accumulation with cyst formation, often focal gitter-cell collections, calcium deposits in some of the areas of necrosis, and areas of only partial destruction of tissue. The blood vessels were on the whole intact, but endothelial swelling was sometimes present, and often the perivascular spaces were filled with macrophages and mononuclear cells.

The features recorded in our case correspond well with those previously reported. Variations in the location and extent of the lesions have occurred from case to case. The outstanding variation in the present case consisted in extensive involvement of both the gray and the white matter. The pathogenesis of the encephalomalacia is not clear.

References

1. Stevenson, L. D., and McGowan, L. E.: Encephalomalacia with Cavity Formation in Infants, Arch. Path. 34:286 (July) 1942.

2. Lumsden, C. E.: Multiple Cystic Softening of the Brain in the Newborn, J. Neuropath. & Exper. Neurol. 9:119 (April) 1950.

3. Winkelman, N. W., and Moore, Mathew, T.: Progressive Degenerative Encephalopathy, Arch. Neurol. & Psychiat. 48:54 (July) 1942.

4. Marburg, O., and Casamajor, L.: Phlebostasis and Phlebothrombosis of the Brain in the Newborn and in Early Childhood, Arch. Neurol. & Psychiat. 52:170 (Sept.) 1944.

5. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood, and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1952, p. 363.

6. Negrin, J.; Lepow, H., and Miller, B.: Multilocular Encephalomalacia, J. Neuropath. & Exper. Neurol. 11:62 (Jan.) 1952.

7. Diamond, I. B.: Encephalomalacia in Infants, Arch. Neurol. & Psychiat. 31:1153 (June) 1934.

Postnatal and Natal Cerebral Injuries

Neuropathological and Neurosurgical Aspects

CLEMENS E. BENDA, M.D.
and
GIAN-FORTUNAT HOESSLY, M.D., Waverley Mass.

Among the causes of mental inadequacy, retardation, and conditions often termed "cerebral palsies," a significant role is played by brain injuries due to mechanical, hemorrhagic, or anoxic factors (oxygen lack, anemia, stagnation). A recent observation on the influence of a head trauma on the mental development of a child impressed us again with the necessity of obtaining more insight into the late effects of injuries to the brain.

Report of Cases

CASE 1.—A 5½-year-old boy was seen at an outpatient clinic because of some behavior difficulties. In the psychological examination he scored a mental age of 6½ years and an I. Q. rating of 116. A few weeks after the examination he was hit by a car and had multiple skull fractures with contusion of the brain. When tested four months after the first examination, the child showed evidence of "cerebral palsy" with hemiplegia. His mental age at that time was 5½ years and his I. Q. rating 93.

Three years later the boy was again examined, at which time he showed complete arrest of mental development at the level which he had reached when the accident occurred. His mental age was 5 years 10 months and his I.Q. rating 69. There was evidence of spastic hemiplegia, and the boy was irritable, excitable, and unpredictable.

The patient is still alive, but observations since 1950 indicate that there is increasing mental deterioration, with increasingly irrational behavior, which may necessitate eventual admission to a mental hospital.

A study of 258 autopsies[1] of mentally defective patients with severe neuropsychiatric lesions revealed that 24% of the cases could be traced to paranatal injuries. The clinical diagnosis in most of these cases was cerebral palsy. This term has found widespread acceptance among pediatricians and orthopedic physicians but is often deplored by neurologists because no uniform pathology is behind the clinical manifestations and no generally accepted definition is available.

The term "cerebral palsy"[2] is used in this study to designate interference with motor control as a result of central pathology, in contrast to infantile paralysis of a spinal type. If properly distinguished from the prenatal developmental disorders, the term encompasses paranatal injuries, fetal erythroblastosis, and postinfectious conditions.

There is a relatively small number of careful follow-up studies of brain-injured children in which sufficient material is available with regard to the type of injury, early management, progressive development of severer symptoms, and neuropathological studies of the final outcome. Cases of this type pose many important problems. Why does a single accident (from which the child apparently recovered) result in progressive mental deterioration, blindness, and increasing neurological symptoms instead of a stationary condition? What are the reactions of the brain and its sheaths to a single injury which

Received for publication March 8, 1956.

Director of Research and Clinical Psychiatry, Walter E. Fernald State School, Waverley, Mass.; Instructor, Harvard Medical School; Lecturer, Tufts University School of Medicine; Assistant Professor, Clinical Psychiatry, Boston University (Dr. Benda). Trainee in Neuropathology Research Laboratory, Walter E. Fernald State School, by grant of National Institute of Mental Health, U. S. Public Health Service; formerly Fellow in Neurosurgery, Lahey Clinic, Boston (Dr. Hoessly).

could explain the seriousness of the late effects so different from the results of a brain injury seen in adults?

A case in which a pathological study was possible two years and nine months after the accident answers some of these questions and offers an understanding of those cases of birth injury in which we find similar brain pathology.

CASE 2.—On April 13, 1951, an 18-month-old infant fell about 30 ft. from a second-story porch to a cement sidewalk and was picked up, unconscious, and brought to a hospital within 30 minutes. The physical examination showed a well-developed and well-nourished little boy, comatose, with arms and legs in rigid extension. At intervals he yawned, sighed, made long, quiet expiratory cries, had slightly stertorous breathing, turned his head from side to side, thrashed his arms about, but did not move his trunks or legs. Abrasions were found in the right frontal region, and a hematoma in the right frontoparietal area. The pupils were first dilated, later small. There was blood on the nose. Four upper incisors were loose, with bleeding from the gums. There were spasms of the jaw. The neurological examination showed hyperactive knee jerks and bilateral plantar reflexes. The provisional diagnosis was abrasions and hematoma of the scalp; fractured skull; contusion of the brain; (?) laceration; (?) hemorrhage, (?) epidural or subdural. X-rays of the skull revealed considerable soft-tissue swelling of the scalp, and a linear zone of diminished density extending obliquely anteriorly and superiorly to the posterior parietal bone. The exact lateralization of this was not determined at the examination, but it would appear to have been in the left parietal region rather than in the right. Impressions were (1) lateral hematoma of scalp at vertex; (2) apparent diastasis of sagittal suture; (3) probable linear fracture, left parietal region. The child was seen by a neurosurgeon within two hours, having developed generalized convulsions. Burr holes were made, and a right subdural hematoma was evacuated. There was some fluid accumulation on the left side also, and contusions and lacerations of the cortex were visualized.

On May 1, the child's physical condition seemed to have reached a point of stabilization. He was able to take fluid from a bottle and strained food from a spoon, and there was no gagging or choking. He was able to turn his head from side to side and move his right arm and leg fairly well, but the left leg poorly and the left arm hardly at all. He could not hold his head up but could put his right arm into his mouth at will. He blinked his eyes to bright light. He had very much the behavior of a 3- to 4-month-old baby.

The child was discharged on May 4, apparently improved, but was readmitted on May 11 with the provisional diagnosis of recurrent subdural hematoma(?). Several lumbar punctures were done, and on May 12 the fluid was clear and colorless, the pressure was 100 mm. when the child was quiet and 200 mm. when crying, and the cytology and chemistry were normal. He was discharged on May 12 with the final diagnosis of contusions and lacerations of the brain, healing; spastic hemiplegia; blindness, and mental retardation.

Four months after the accident, a neurological examination showed that the scalp wounds had healed well. There was moderate flaccidity of the neck muscles. The patient did not open his eyes fully; the pupils were approximately 3 mm. in diameter. There was slight weakness of the left arm and leg as compared with the right, and a bilateral Babinski sign, more definite on the left than on the right side. The parents stated that the child had begun to use his extremities more actively in the preceding weeks and rolled about quite actively in his crib, though unable to sit or stand up. (Prior to the accident he had been able to walk quite well.) He still used his left arm and leg much less than the right. He took feedings well and slept well. He had periods of crying for no apparent reason. He did not appear to see any objects and gave no signs of recognition of his parents by sight. The hospital summary was as follows: "The patient's present condition appears to be due to generalized cerebral injury, including brain-stem damage. He has shown slight improvement since the last examination, and there is no evidence at present to warrant further diagnostic studies."

Six months later the parents reported marked improvement. They thought the child had equal use of both legs, and the left arm had improved, although it was still moving less than the right one. He was now able to raise his head from the bed, and was able to sit up with support and roll from side to side in his crib. The parents thought he was unable to see, and there was question whether he recognized the voices of his parents. He made no attempt to walk or talk. On neurological examination, the child still showed evidence of left-sided weakness. The pupils reacted to light, but the child did not follow light. He did not grab any objects, even when close to his hand. It was the opinion of the hospital staff that the outlook was grim: "This boy may develop better muscle power in the future, but his higher brain functions are nil."

On May 13, 1953, when 3 years 7 months of age, this child was seen by one of us (C.E.B.) for the first time at the outpatient clinic of the Walter E. Fernald State School, two years and one month after the accident. The boy was blind, lay huddled

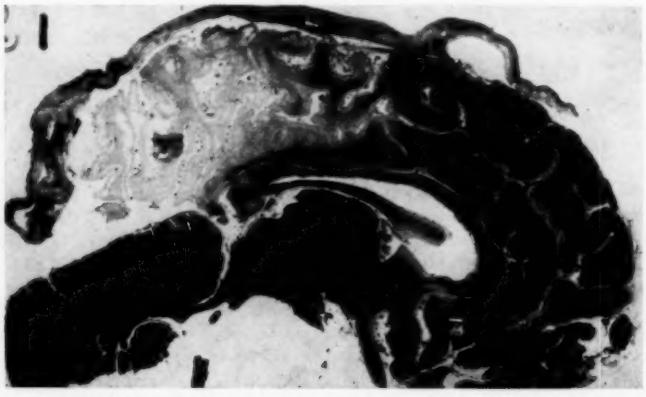
in a fetal position, and sucked his thumb until approached by the examiner. He whimpered softly when spoken to and wailed pitifully when his position was changed or any object was placed in his hand. Any outside interference seemed terrifying. There was no indication of his intellectual potentials, and he could not cooperate in the simplest of tests.

The boy was admitted to the Fernald School, where he spent all his time in a crib, showing evidence of spastic rigidity of all extremities, blindness, and no reaction to light. He was very irritable and resisted any handling. He died rather suddenly on Jan. 5, 1954, at an age of 4 years 3 months; the diagnosis was hemorrhagic enteritis.

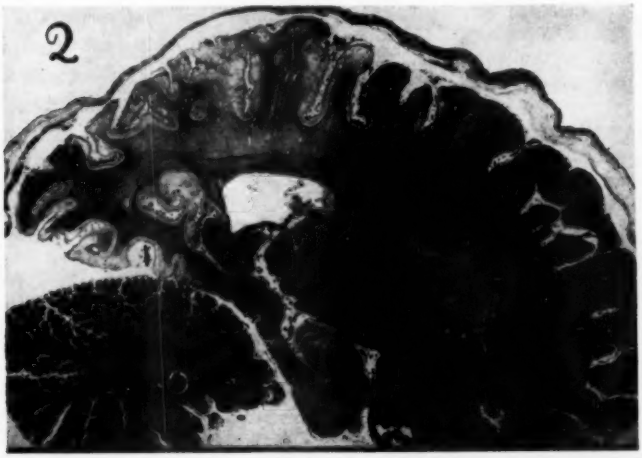
At autopsy the head was found to have a circumference of 19½ in. (49.5 cm.) and showed a scar on the left side of the skull, with a depression on the parietal bone above the left ear and depressions on the right parietal bone. There was slight ptosis on the left, in contrast to the right. Both fists were clenched and the wrists flexed. The right foot was in an equinovarus position and stretched; the left foot, in a more retroflexed position. After the scalp was retracted from the calvaria, the skull bone revealed scars from the burr holes and a scar in the frontal bone beside the midline in front of the coronal suture, and bilateral depression of the parietal bones behind the coronal suture. The skull bone was very thick. The frontal bone measured up to 1 cm. The sutures were firmly closed; the dura was very much thickened and showed duplication of the inner layer. There was still evidence of a large, organized subdural hematoma over both hemispheres in the occipital, parietal, and postcentral areas. There were adhesions between the pia-arachnoid and the dura. In the left occipital region, the sheaths of the dura were separated by a large cyst, which depressed the occipitoparietal region. Over the right occipital lobe there was an old organized subdural hematoma, which depressed the occipital convolutions. The optic nerves were ensheathed in a reddish fibrous tissue. The brain weighed 820 gm., including the greatly thickened dura. Both occipital lobes showed extensive laceration of the brain tissue. No developmental anomalies were found.

The two hemispheres were separated by a sagittal midline section. In this way the extent of the subdural hematoma could be well demonstrated. The dura was of an abnormally white color and greatly thickened, the outer layer alone measuring 2 mm. in thickness. Behind the sulcus of Rolando there was a large organized subdural hematoma, which was walled off against the brain by another thickened membrane, measuring 2 mm.

Figs. 1-3 (Case 2).—Sagittal sections through right hemisphere (Weigert myelin stain). Section 1, about 0.5 cm. from midline; Section 2, 1.5 cm. from midline; Section 3, 3 cm. from midline.



Section 1: Greatly thickened dura around parietal and occipital lobes. At the occipital pole, the inner sheath of the dura is greatly proliferated and a large pocket which had contained fluid has formed within the dura. The occipital convolutions beneath this pocket are especially severely degenerated. The cortex is reduced to a thin strip of gray matter, under which gray and white matter are separated by a continuous number of smaller and larger cysts with some interspersing fibrous tissue. The cysts contain some fiber organization and numerous gitter cells. The occipital pathology explains the cortical blindness which the child developed about three months after the accident. The same type of pathology is found throughout the occipital lobe and parts of the parietal lobe, where remnants of myelination can be observed in the white cores. The convolutions are "microgyric," or, rather, sclerogyric. In the frontal lobe, there is evidence of some demyelination and sclerosis as after-effects of the brain contusion. The pathology in the frontal lobe is, however, far less severe than in the parietal and occipital lobes.



Section 2: Cortical encephalomalacia, most strikingly in the parietal-occipital region and at the lower aspect of the occipital lobe. The dura is greatly thickened, even above the precentral and frontal convolutions. The posterior, central, and precentral convolutions show various stages of cortical encephalomalacia, which apparently was progressive but not as much advanced as in the occipital and parietal regions.

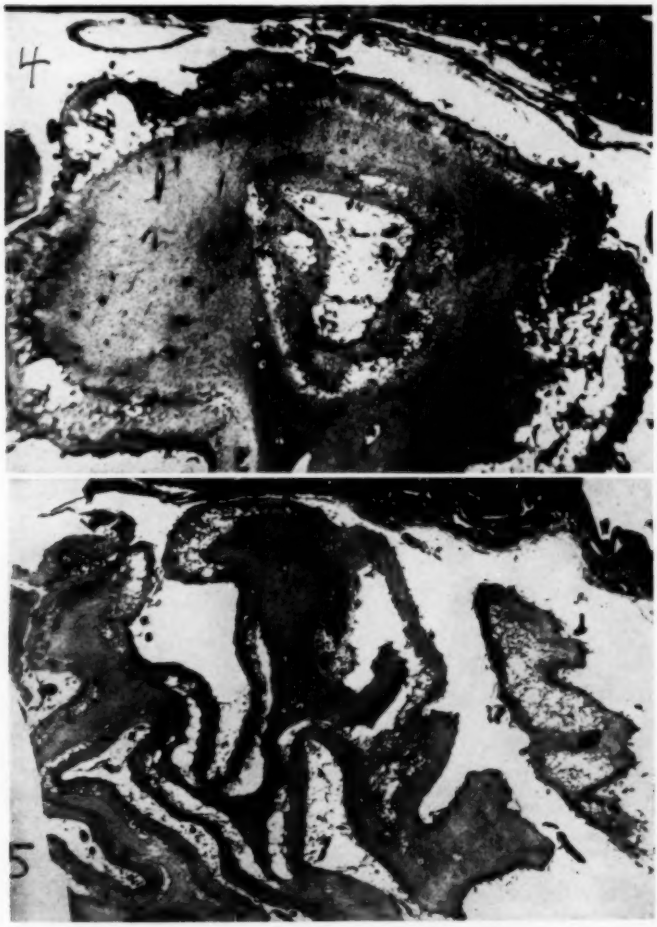
Section 3: Pathology similar to that seen in Section 2, but again a fluid pocket over the occipital area, beneath which the degeneration of the brain is more conspicuous.

The walls of the superior longitudinal sinus were greatly thickened, resulting in a narrowing of the lumen of the sinus. There were some organized blood clots visible within the sinus. Although a certain amount of recanalization was noticeable, the passage ranged from narrow to complete obliteration. The falx itself showed proliferation and residues of old organized hemorrhages on both sides. The left hemisphere revealed fairly normal convolutions in the frontal, temporal, and parietal areas, but the whole occipital lobe showed microgyria. The convolutions were shrunken and sclerotic. Examination of the ventricle showed that it was moderately enlarged.

The right hemisphere appeared grossly similar to the left one, with the main pathology in the parieto-occipital lobes. In addition, there were microgyria and evidence of general contusion in the frontal lobe, which will be described later. A number of sagittal sections, placed about 1 cm. apart, were embedded in celloidin, cut by a hemisphere microtome, and stained by the methods of Weigert and Nissl. In addition, smaller sections were stained by the Van Gieson method, hematoxylin-eosin, and some silver methods. The stained sections showed clearly the greatly thickened dura with an organized subdural hematoma, beneath which was another greatly thickened membrane. The convolutions of the brain behind the central sulcus were demyelinated and showed extensive subcortical encephalomalacia and cystic degeneration of the white matter. Large areas of the subcortical white matter were found to be completely destroyed and replaced by cysts filled with gitter cells and a network of mesodermal fibrous tissue.

Sections stained after the Van Gieson method show clearly not only the cysts filled with mesodermal fiber tissue but the walls of the capillaries increased in thickness and the perivascular spaces organized by fibrous tissue. The white and gray matter reveal a proliferation of mesodermal tissue

throughout, which penetrates the white and gray matter, replacing nerve parenchyma and invading the cysts. There are only strands of cortical tissue left, islands with few nerve cells preserved, all of which are in a state of severe degeneration.



Figures 4-5 (Case 2). —Higher magnification of occipital lobes (elastica Van Gieson stain). The black tissue at the top of the sections is a thickened dura. The subarachnoid space is mostly obliterated. The gray matter is severely degenerated and reveals a thick glia felt throughout. The gray matter is separated from the white matter through fluid spaces which show fibrous organization. The pockets contain numerous gitter cells. The capillaries in the white matter are greatly proliferated, and a fine network of mesenchymal tissue has proliferated through the whole white matter.

More laterally placed sagittal sections show that the destruction involves the whole parieto-occipital lobe; and the subdural hematoma, with a thickening of the sheath, covers the whole convexity. A new feature appears in the frontal lobe, where there is an encephalomalacia of the frontal pole. There is demyelination, encephalomalacia, and formation of small cysts.

The pathology described above is identical with that found in a number of cases which we consider instances of paranatal injuries. Four cases of cystic degeneration with the clinical manifestations of Little's spastic rigidity have been described by one of us (C.E.B.).* Seven additional cases of cortical encephalomalacia were observed. One case in particular had almost identical clinical manifestations, but the patient died four and a half months after birth.

Case 3.—The boy was one of dissimilar twins, the twin sister being in good condition. The boy is said to have been dropped by a nurse on the second day after birth, although it was impossible to ascertain the truth of this statement. The birth history was negative, however. A twitching of the right upper and lower extremities was observed on the third day after delivery, and a semicomatose condition developed. The twitching continued for several days, and food had to

* Benda,[2] pp. 239-241, 246-249.

be given by an eyedropper. The head began to enlarge on the 10th day after birth. On the 15th day the twitching ceased, but spasticity of the arms and legs was noted. A month after birth the child appeared to be blind, the pupils did not react, and bilateral nystagmus was present. At an age of 3 months the child's head seemed disfigured, with a depression of the right frontal bone and overlapping of the left skull bones over the right side. There were quadriplegia and paralysis of the left external eye muscle with strabismus and nystagmus; the pupils were unequal, and the child was blind.

At autopsy a large epidural and subdural hematoma was found, with multiplication of the dura sheath. A large blood clot covered the convexity of the brain, which showed a severe degree of cystic degeneration.

Six new cases, observed since 1952, are summarized in the accompanying Table. Two cases are presented in more detail.

CASE 4.— Patient E was the second of two pregnancies, full term, delivery instrumental, with high forceps. Shortly after delivery, the attending physician noticed cyanosis and convulsions and suspected a cerebral hemorrhage. From the time of birth the child had frequent convulsions and was listless and helpless. He appeared to be blind. He had spasms when lifted but usually lay quietly, without turning. He could not grasp any objects. At an age of 2 years 7 months the child was an obese, good-natured infant who could not see except to the extent of distinguishing light from dark. He could sit up momentarily in the examiner's arms but would suddenly stiffen and become rigid. He made no sounds but smiled occasionally.

At an age of 3 years, the child had a head circumference of 18 in. (45 cm.). There was opisthotonos; the eyeballs often rolled upward; the arms were flexed and spastic; the right leg was flexed and spastic, the left one extended. The child had numerous seizures in which the legs were stretched and the arms made short, clonic movements while the head was drawn backward. The neurological diagnosis was microhydrocephaly due to brain injury at birth; cystic degeneration of the brain.

During the following years the child became increasingly rigid, with occasional temperature

*Cases of Cystic Degeneration in Second Research Series, of 131 Cases**

Patient	Age† Sex	M.A.	I. Q.	Family History	Birth	Early Manifestations‡	Clinical Symptoms	Pathology
A	18 yr. M	0 yr.	0.07	Negative	"Normal"	Cried continuously at 7 mo.; no speech	Seizures; severe mental deficiency; aphasia; paratonic rigidity; head banging; "psychotic" behavior patterns	Cranial dysostosis; hemiatrophy, left hemisphere; cystic degeneration, temporal lobe; old subarachnoid hematoma, left hemisphere; thrombosis in left cortical vein
B	5 yr. F	0 yr.	0.09	Negative	Cord around neck; asphyxiation	Convulsions at 9 mo.	Spastic tetraplegia	Brain weight, 500 gm.; cystic degeneration; internal hydrocephalus
C	6 yr. M	0 yr.	0.10	Negative	High forceps; injury to forehead; asphyxiation; convulsions	Microcephaly; blind (?) ,no walking, poor speech	Blindness; rigidity; no walking; no talking	Brain weight, 915 gm.; cystic degeneration, occipital poles; enlarged ventricles; organized subarachnoid hemorrhages
D	2 yr. F	0 yr.	0.13 est.	Negative	Full term, very difficult; cyanosis; 3 wk. in incubator	At 3 mo. no head growth from previous month	No walking; no speech; strabismus; spasticity and rigidity, all extremities	General microgyria and sclerogyria, both occipital lobes; enlarged ventricles; thickening of sagittal sinus; bilateral subdural hematoma
E	6 yr. M	0 yr.	0.08	Negative	High forceps; cyanosis; convulsions	No walking; no speech; blind; convulsions since birth	Helpless; continuous seizures; extremities spastic; increasing rigidity	Generalized cystic degeneration; subcortical encephalomalacia; old extradural hemorrhage
F	14 yr. M	?	?	Negative	Twin; other nonviable; full term	No history	Helpless; no walking; no speech; spastic diplegia; contractures; microcephaly	Focal cystic lesions; organized blood in dura (?)

* From Walter E. Fernald State School.
† "Age" refers to age at the time of death.
‡ Early manifestations are taken from the history before hospital admission, which was often rather unsatisfactory.

rises. In spite of large doses of anticonvulsive therapy, he continued to have seizures. He died in 1953, at an age of 6 years and 10 months.

At autopsy, the calvaria was noted to be very thin. After removal, the dura appeared wrinkled, and there was some organized hemorrhagic exudate epidurally. The brain showed a severe cystic degeneration which involved a large part of the convexity. The frontal lobes showed microgyria. In the temporal lobes the convolutions were completely destroyed, and only remnants were found near the midline, where the convolutions were again sclerogyric. About the occipital poles the brain showed a cystic degeneration. The weight of the whole brain, including the cerebellum (which appeared normal), was 335 gm.

The microscopic slides reveal a very severe cystic degeneration and cortical encephalomalacia. The frontal, precentral, and parietal lobes are almost completely destroyed. The lateral ventricles are greatly enlarged. The only preserved tissues are the medial aspects of the occipital lobes, whereas the lateral convolutions are destroyed and show different stages of cystic degeneration of the white matter, with fibrosis and numerous gitter cells. The white matter is either destroyed or shows various stages of demyelination.

Case 5.—D's birth is said to have been at full term, by a very difficult delivery. She was blue and had spells of cyanosis. She was kept in an incubator for three weeks. When she was 3 months of age, it was noticed that her head circumference had not increased since the previous month. She did not develop mentally and made no attempt to move around. A neurological examination established strabismus and spastic rigidity of the arms, legs, and entire body. The child cried frequently as if in pain, stiffened, and jerked her head, but did not lose consciousness. She smiled often. When she was seen in our outpatient clinic, at an age of 21 months, her head seemed moderately microcephalic and there was decerebrate rigidity of the body and extremities.

D was admitted to the institution at an age of 24 months. At that time she was a plump, attractive girl, who was unable to sit up unsupported. She did not follow objects with her eyes, and her vision was questionable. She was easily startled and kept her hands in a clenched position. She was a severe feeding problem and lived only four months after admission.

At the time of autopsy the child was 2 years 4 months old and measured 78 cm. (30¾ in.) in length. The head circumference was 39.7 cm. (15¾ in.). She was a rather delicate-looking child with fine features. The eyes were large, the pupils wide and asymmetrical in size. The body was well formed, but the legs showed a congenital dislocation of the hips, which was confirmed by x-ray examination. The calvaria was thin and ossification was not regular, with some translucent areas where the membranous skull was little ossified. The whole brain weighed 430 gm. The convexity showed evidence of microgyria and sclerogyria in both parietal and occipital lobes and many sclerogyric convolutions on the convexity. The dura showed definite evidence of subdural hematomata on both sides, but especially severe on the left side near the sagittal sinus toward the occipital pole. The sagittal sinus was fibrotic.

Illustrations of the microscopic examination of the brain demonstrate the great enlargement of the lateral ventricles, with the white matter reduced to a thin strip. The convexity of the brain shows a few normal convolutions in which myelination is quite well developed, but the majority of the convolutions are reduced in size, the white core is demyelinated, and toward the parietal and occipital poles the convolutions are destroyed. There is encephalomalacia and cystic degeneration throughout.

Fig. 6 (Case 5).—Occipital pole of right hemisphere below the greatly enlarged lateral ventricle. The optic radiation shows severe demyelination. The lips of the calcarine fissure to the right show demyelination and gliosis. The convolutions are of a sclerogyric type. The white matter shows numerous smaller and larger cysts, with fibrous organization and gitter cells.

Case Analysis

An analysis of the histological features of a child who died 2 years and 9 months after a severe brain injury demonstrates clearly the way in which the brain reacted to such a trauma. Reconstructing the events that occurred at the time of the accident: The child fell from a porch to the cement sidewalk and apparently hit the ground with the forehead first, and the brain was thrust against the frontal bones by the force of

inertia. Microscopic sections near the midline demonstrate the contusion of the frontal pole and lower surface of the frontal lobe. This brain damage was caused by the direct impact of the fall. Severe as this brain damage is, it is far less extensive than the pathology of the parieto-occipital lobes. The posterior third of the brain shows severe demyelination of the white matter and cortical and subcortical encephalomalacia, with small cysts in the white matter and sclerogyria of the convolutions. The pathology is severest near the medial aspect of the occipital lobe but extends to the lateral convexity of the brain. Evidence of a subdural hematoma is found extending over the whole convexity. The dura shows proliferation over the entire prefrontal areas. The dura is relatively thin over the parietal lobes, and yet cortical encephalomalacia is striking in this area. The lateral sections provide evidence that there was a cystic dural sac over the occipital lobe and a large proliferation of the dura at the very caudal end of the brain.

We have to assume that the neurosurgical removal of the fresh and moderately organized hematomata in the parieto-occipital area succeeded in reducing some of the subdural hematomata. It did not succeed, however, in preventing the formation of a cystic sac under the dura, which was filled with fluid and compressed the brain like a water cushion. We have to assume, further, that the severe encephalomalacia was due to the tearing of the bridging vessels. The severance of connections prevented adequate venous drainage in these areas. At the same time, the arterial supply was greatly reduced through damage to the smaller arteries and compression of the area by the hemorrhage and fluid accumulation through brain edema. The dura at autopsy appeared greatly thickened over the whole convexity, with evidence of organized hemorrhages and fluid cysts within the dural sheath. Although the child was operated on immediately after the accident, at which time the fresh bleedings were removed, either new bleedings occurred at later periods or certain areas could not be reached. The early operation did not prevent the formation of new membranes. Treatment was entirely conservative after the first operation, and no attempts were made to remove later bleedings or to reduce the membranes and fluid accumulations.

How far the brain tissue can recover in a contusion is questionable, but the additional factors of interference with circulation and nutrition cause a progressive degeneration of brain tissue, consisting of an encephalomalacia and cystic degeneration of the white matter. Figures 1 to 3 demonstrate in which ways the different areas of the brain were affected. It is worth noting that the actual damage caused by the contusion in the frontal area is less severe than the pathology which developed as a result of indirect factors in connection with the accident.

The microscopic study reveals extensive proliferation of mesodermal tissue within the brain, arising from the vascular system. The scar formation far exceeded the usefulness of organization, and in this connection it may be useful to call attention to Richards' concept[3] that Nature does not operate only under the law of homeostasis (the tendency to restore a state of equilibrium) but that the forces of reparation often overshoot their goal. Extensive scars result in a strangulation of the tissues, which process Richards terms "hyperexis" ("having too much").

Comment

The observations made in Case 2 throw light on a number of similar cases in which, however, the injury occurred earlier in life, usually at the time of birth or shortly after.

A perusal of our entire institutional autopsy material, now comprising 331 cases of various types of mental disorders of childhood observed since 1936, shows the following:

Ten cases revealed severe cystic degeneration of the white matter. In the first series, of 200 cases,[2] 7 cases showed extensive sub-

cortical encephalomalacia with severe destruction of cortical layers but less involvement of the white matter. The number of instances of subcortical encephalomalacia in the second series, of 131 cases, has not yet been determined. Needless to say, not all cases of apparent cystic degeneration are due to birth traumata, and we are fully conscious of the prenatal developmental disorders which may result in a very similar pathology, often classified as porencephalies.[4]

In Cases 3, 4, and 5 we found a uniform neuropathology. Without drawing unwarranted conclusions, it seems safe to assume that the brain was exposed to deformation of the skull without fracturing, but resulting in tears of subdural and bridging veins and contusion of brain tissue. There was actual evidence of subdural and subarachnoid hemorrhages, which exercised a constricting, inhibiting influence upon brain circulation and nourishment through a "cushion" mechanism. Our case of postnatal trauma seems to indicate that cystic degeneration and encephalomalacia develop through circulatory insufficiency and asphyxiation, rather than as a result of direct contusion.

Space does not permit dealing with the extensive literature about birth injuries which, starting with Denis (1826), Billard (1828), and Cruveilhier (1829), includes many of the best-known names in pathology and obstetrics: Virchow (1867), Kundrat (1891), Seitz (1907), Benecke (1910), Ylppoe (1919), Schwartz (1924), Ford (1926), Naujoks (1934), Kehrer (1939), and Spatz (1939). Most of these studies deal with the immediate effects of birth traumata, however, and the late effects of birth injuries are not often discussed. One of us (C. E. B.) gave accounts of it in 1945,[5] and again in 1952.[2]

The literature, as well as our own material, indicates that an injury to the brain should not be considered a single event after which more or less restoration may occur if the initial damage, with its effects, has been successfully treated. It must be emphasized that traumatic influences upon the brain of the newborn and infant present a problem that is quite different from and more serious than injuries occurring in adults. The injury affects an organ still in the process of growth, development, and maturation. Injury—whether circulatory, nutritional, or due to asphyxiation—not only results in pathology of a focal type with loss of some physiological function but interferes with the entire process of maturation and differentiation. Thus, a single injury of limited duration may result in an interruption of development with irreversible focal pathology, inhibition of further progress with hypoplasia, and interference with the potential function of the rest of the brain, which had not been directly exposed to the injury.

It seems imperative that the process of brain injury in early life be well understood by pediatricians, neurosurgeons, and pathologists because the particular conditions of infancy call for specific approaches not common to those who deal mainly with adult patients. Although subdural hemorrhages have attracted the interest of neurosurgeons and neurologists on a large scale, very few have pointed out the importance of subdural hemorrhages in the newborn and young child and shown how much can be accomplished in such cases through early diagnostic and surgical intervention.

In 1946, Morf † called attention to the very interesting fact that mature newborn infants are apt to suffer from tentorial tears in cases of birth injury, while the premature child is characterized by bleedings from the vena terminalis and its tributaries. He called attention to involvement of the fetal matrix surrounding the vena terminalis, which is not yet matured at the time of premature birth and suffers damage through venous hemorrhages. The pathology of the matrix results in abnormal development of the subependymal layers which

† Morf, H.: Beitrag zur pathologischen Anatomie und Pathogenese der Vena terminalis: Blutung bei Neugeborenen, Thesis, Medical Faculty, University of Zurich, 1946.

surround the ventricles and cover the caudate nucleus.

In 1939, Ingraham and Heyl [6] pointed out the difference between subdural hematomata existing in adults and those in young children. They called attention to the fact that the brain volume is approximately doubled in the first three months of life and doubled again in the following six months. They stressed the point that even a thin membrane of unflexible connective tissue resulting from an organized subdural hematoma will produce irreparable damage in constricting the expanding brain and preventing further normal maturation, in contrast to the adult brain, which had previously attained its full volume.

In addition to these "constrictive effects," many writers have called attention to the diminished absorption of cerebrospinal fluid through obliteration of the subarachnoid spaces, through inflammatory reactions secondary to the presence of blood, and through venous stasis which interferes with drainage of blood from the nervous system itself. The organization of hematomata and membranes often produces pockets of fluid filled with clear yellow exudate, which increase in size, fluctuate in their volume, and act like a water cushion upon the hemispheres of the brain.

There is general agreement that early and active intervention is necessary. Repeated subdural taps through the coronal suture lines are recommended, attempts at early removal of hematomata being made before a membrane has been formed. In cases of excessive subdural fluid obtained from these taps, bilateral temporal burr holes are indicated. Exploration for the presence or absence of subdural membranes should be made. If a membrane is found, bone flaps have to be made for removal of the membrane as completely as possible.

One of us (C. E. B.)[2] has called attention previously to the fact that the birth-injured newborn usually shows symptoms of brain damage within the first 48 hours by irritability, seizures, crying spells, circulatory spells, and feeding difficulties. In a recent publication by Schipke, Riege, and Scoville,[7] the necessity for early diagnosis and active intervention has been reemphasized. They restate the early symptoms referable to the cardiorespiratory system. We may quote their summary as especially useful‡:

> Varying degrees of cyanosis are common. Pallor is peculiarly striking and probably represents a form of "shock," either directly from blood loss or because of insult to the brain. In general, some degree of asphyxia will be present at birth. In many cases a temporary period of apparent improvement will follow, particularly in those infants surviving the first 24 hours of life.
>
> The facial expression may be the first indication of an intracranial injury. A painful wrinkling of the brow expressing anxiety or an unusual alertness, with eyes wide open and staring is often noticeable. Feeding difficulties arise early, although the sucking reflex usually remains intact. Restlessness, irritability or listlessness will be present. Neurological changes such as unilateral or bilateral flaccidity or spasticity can appear, early or late, depending upon the severity and extent of hemorrhage. Unequal pupils and lateral deviation of the eyes are very significant, and occur relatively early. Twitching is common and usually begins around the mouth and then becomes generalized. Changes in the deep tendon reflexes will depend upon the degree of motor involvement. An absent Moro reflex at birth is suggestive of cerebral edema rather than hemorrhage; however, if the Moro reflex is normal on initial examination and then becomes asymmetrical or disappears, intracranial hemorrhage is likely. Anemia, sweating, fever and jaundice may be found but are of little diagnostic value.

The histories of brain-damaged children usually indicate that oxygen is the only treatment which most of these newborn infants receive. The routine use of oxygen has misled physicians to the belief that its application is the safest procedure and an adequate therapy in the management of cerebral birth injuries. It may, however, be suspected that prolonged oxygen inhalation without any other therapy is not without harm in cerebral hemorrhages. Oxygen produces enlargement of certain circulatory areas and constriction of others, bringing about a severe change in blood and cerebrospinal fluid pressure and producing hyperemia in some areas and anemia in

‡ Schipke and others,[7] p. 469.

others. It is likely that the tendency to bleeding is actually increased under oxygen, while the symptoms are obscured by the very fact of survival. The formation of scars and other reparative processes may take a different course under oxygen, as is suggested by the occurrence of retrolental fibroblastosis in the premature child.

From a neurological-neurosurgical point of view, it seems evident that the treatment of brain-injured newborn infants and older infants needs to attract the attention of a larger group of investigators, who may be able to develop new and more efficient methods of approach.

Summary

Among the causes of mental disorders of childhood, so-called "cerebral palsies," blindness, and mental deterioration, a considerable role is played by injuries to the brain at the time of birth and early in life.

The case of an 18-month-old infant who fell 30 ft. from a second-story porch to a cement sidewalk and developed unconsciousness, paralysis, and finally blindness is presented in detail, with neurosurgical procedures immediately after the accident and clinical and neurological observations over a period of 2 years and 9 months, to the time of death, after which a careful neuropathological study was made. The child revealed evidence of the late effects of a concussion of the frontal lobes, and severe encephalomalacia and cystic degeneration of the whole occipital and parts of the parietal lobes, in connection with a greatly thickened dura and formation of fluid sacs within the dural sheaths. The mechanism and significance of this pathology are discussed.

Two cases of paranatal injuries and one of a brain trauma a few days after birth, with similar pathology, are presented and a summary given of six cases of cystic degeneration of the brain.

Birth injuries and traumata early in childhood are serious because the lesions interfere with a rapidly growing brain, the development of which is constricted and the immature brain tissue deprived of proper circulation and nutrition, undergoing rather rapid degenerative changes. Among the neuropathological lesions, cystic degeneration of the white matter and encephalomalacia of the gray matter are both most conspicuous. The progressive character of the lesions explains the progressive deterioration and the gradual development of blindness observed in several of these cases.

The early diagnosis of brain injuries in infancy and childhood is discussed, and a more active neurosurgical approach is suggested.

REFERENCES

1. Benda, C. E.: Structural Cerebral Histopathology of Mental Deficiencies, Proceedings of First International Congress of Neuropathology, Torino, Italy, Rosenberg & Sellier, 1952, Vol. 2, pp. 7-50.

2. Benda, C. E.: Developmental Disorders of Mentation and Cerebral Palsies, New York, Grune & Stratton, Inc., 1952.

3. Richards, D. W.: Homeostasis Versus Hyperexis: or Saint George and the Dragon, Scientific Month. 77:289-294, 1953.

4. Yakovlev, P., and Wadsworth, R. C.: Double Symmetrical Porencephalies, Tr. Am. Neurol. A. 67:24-28, 1941.

5. Benda, C. E.: The Late Effects of Cerebral Birth Injuries, Medicine 24:71-110, 1945.

6. Ingraham, F. B., and Heyl, H. L.: Subdural Hematoma in Infancy and Childhood, J. A. M. A. 112:198-204, 1939.

7. Schipke, R.; Riege, D., and Scoville, W. B.: Acute Subdural Hemorrhage at Birth, Pediatrics 14:468-474, 1954.

Statistical Control Studies in Neurology

VII. The Oppenheim Sign

M. J. MADONICK, M.D., New York

In view of the rather meager body of data concerning the incidence of the Oppenheim sign, two large groups, one of patients and one of healthy people, were studied to determine the frequency and significance of this sign.

Oppenheim [1] described the sign in 1902. The technique employed by him consisted of vigorous stroking of the inner aspect of the leg along the posterior edge of the tibia with the handle of the percussion hammer, beginning just below the knee and ending at the ankle. In healthy people no movement or a plantar flexion of the big toe, and sometimes of all the toes, was produced. In affections of the pyramidal tract there was dorsiflexion of the big toe and sometimes of all the toes. Oppenheim examined 76 patients with neurasthenia, hysteria, hemicrania, *tic convulsif*, and similar affections. No dorsiflexion of the big toe was demonstrated. In only two instances, in which all other signs of lesions within the nervous system were lacking, was there a spread of the toes. Of the 574 people examined by Pfeifer,[2] 200 were adults and 64 children with no nervous disorders. Except for six cases in the adult group with no nervous disorders in which dorsiflexion of the big toe and plantar flexion of the remaining toes occurred inconstantly and so quickly that a volitional element was present, no convincing Oppenheim sign was demonstrated. Of the 40 children up to one year of age, the Oppenheim sign was present in 35% and the Babinski sign in 62%. Of the 24 children from 1 to 12 years of age, 5 had the Babinski sign; the Oppenheim sign was present in 3, once bilaterally and twice unilaterally. Cassirer [3] examined 185 patients; 79 had functional nervous disorders. In the test for the Oppenheim sign, 65.8% of the 79 patients showed plantar flexion and in 34.2% plantar flexion was absent or movements of the toes were unclear. No Oppenheim sign was present. Cassirer indicated that the Oppenheim sign was less constant than the Babinski sign. He agreed with Oppenheim that the Oppenheim sign is more frequent in spastic conditions, and he also stated that it may appear before the Babinski sign. Schlesinger [4] examined 640 adults over 60 years of age; the Oppenheim sign was present as frequently as the Babinski but was not found in all instances in which the Babinski sign was elicited. He considered it a valuable sign. Deutsch [5] examined 500 healthy children between 6 and 14 years of age. Of these, 80 had big-toe signs of various strengths and combinations; 33 had the Oppenheim sign, and 9 the Babinski sign. Zhukovski,[6] in describing his toe sign, mentioned the Oppenheim sign as being one of pyramidal tract involvement. Myerson [7] wrote that "while Babinski more frequently occurs alone than either Oppenheim or Gordon, their appearance even without Babinski means organic disease of the cerebral motor neurone and therefore they merit inclusion in the routine neurological examination." Piotrowski,[8] Gordon,[9] and Lewitsky [10] considered the Oppenheim sign an indication of pyramidal tract involvement. Rouquier [11] also indicated that the Oppenheim sign is a pyramidal tract sign but that it is less sensitive and less often observed than the Babinski. Zanuttini [12] exmained 750 healthy soldiers from 20 to 22

Received for publication Feb. 25, 1956.

From the Neuropsychiatric Service of the Morrisania City Hospital.

years of age; in 10 there was slight dorsiflexion of the big toe, in 1 slight dorsiflexion of the left foot and big toe, and in 7 slight dorsiflexion of all the toes. In their textbooks, Nielsen,[13] Purves-Stewart,[14] Wechsler,[15] Monrad-Krohn,[16] and Brain[17] accept the Oppenheim sign as a pyramidal tract sign. Alpers wrote[18]: "It is indicative of corticospinal disease but is not constant; indeed, it is infrequently encountered." Fulton[19] characterized the Oppenheim sign as a withdrawal response to lesions restricted to Area 4 in the chimpanzee and man. Walshe[20] stated that it is the same as the extensor plantar response, which can, however, be elicited from a different part of its wide receptive field. Lassek[21] mentioned that the Oppenheim sign is similar in nature to the Babinski; however, "it is used infrequently as a diagnostic test in comparison to the Babinski." DeJong[22] accepted the Oppenheim sign as a pyramidal tract sign; however, he considered it not as delicate as the Babinski sign.

Material and Methods

Two groups of people were studied.

Group 1 was composed of 2500 patients with non-neurologic disease admitted to the surgical, medical, and obstetrics wards of the Morrisania City Hospital. The age incidence of the group when graphed showed a bell-shaped curve, indicating that the sample was statistically valid. There were 1695 females and 805 males. This ratio is greater than the ratio of 100.6 females to 100 males in the Bronx, according to the Census of 1930. The greater number of females is probably due to the large gynecologic and obstetrical division in this hospital. Negroes comprise 1.02% of the population of the county; of the series of 2500 hospital patients, Negroes constituted 11.6% of those examined. The greater number of Negroes in the series is most likely due to economic conditions and the fact that the hospital is a city institution.

Group 2 was composed of 706 inductees, all male, between the ages of 21 and 35. In the present investigation, the requirement for an Oppenheim sign was dorsiflexion of the big toe, no matter what position the small toes assumed. The method of testing for the sign was that of Cassirer,[3] who substituted energetic pressure with the thumb of the examiner for the handle of the percussion hammer, as employed by Oppenheim.[1] This procedure is less likely to cause irritation and injury to the skin than the reflex hammer handle.

Results of Study

Group 1.—Of the 2500 non-neurologic hospital admissions, 55 had Oppenheim signs, an incidence of 2.20%. Tables 1 and 2 list the cases of the Oppenheim sign with other signs of lesions within the nervous system and without other signs of lesions within the nervous system, respectively. Table 3 summarizes the two Tables. The Oppenheim sign was slightly, but not significantly, more frequent in the females than in the males—2.30% to 1.98%.

Table 4 shows the distribution of the Oppenheim sign according to the age groups in the series of 2500 non-neurologic admissions. It is interesting to note that the incidence of the sign increases with age. Thus, the incidence of the Oppenheim sign rises from 1.28%, in the 20-39-year age group, to 5.54%, in the 60-year and older age group. Increase in the frequency of the Babinski[23] and Hoffmann[24] signs with age were reported in previous studies; however, an increase with age was not observed with the Rossolimo sign.[25] The Oppenheim sign was present in 1.04% of the Negroes, as compared with 2.35% of the white patients. This difference may be partially explained by the greater number of Negroes in the younger age groups. Of the patients in Group 1 with the Oppenheim sign, 65.5% had other signs of lesions within the nervous system. The presence of an Oppenheim sign is thus in favor of nervous system disease; it is a pyramidal tract sign. Whether the Oppenheim sign is due to functional interference or an anatomic lesion in the pyramidal tract cannot be answered without a study similar to that which Nathan and Smith[26] carried out for the Babinski sign. The present investigator confirms the occasional value of Ganfini's[27] maneuver of reenforcement of the Babinski by the Oppenheim sign; such a combined procedure often results in a more evident dorsiflexion of the big toe in instances in

TABLE 1.—*Incidence of Oppenheim Sign in 2500 Cases with Other Evidences of Lesions in the Nervous System*

Age, Yr.	Sex	Race	Unilat.	Bilat.	Diagnosis	Other Evidences of Lesions in the Nervous System
36	F	W	L		Acute bronchitis	Bilateral Hoffmann
70	F	W		+	Cataract	Bilateral Babinski; absence of abdominals; hyperactive reflexes
64	F	W	R		Acute cholecystitis	Right Gordon; right Babinski
32	M	W	R		Hemorrhoids	Left abdominal not elicited
54	M	W		+	Arteriosclerotic heart disease	Bilateral Schaffer; crossed Oppenheim and Gordon
44	F	W	L		Gastrointestinal malignancy	Left Babinski; left abdominals greater than right; left knee jerk greater than right
58	F	W	R		Cancer of uterus	Right Gordon; bilateral Babinski; left abdominals absent
62	F	W	L		Hypertensive heart disease	Left Babinski; left knee jerk greater than right
45	M	W	L		Acute glomerulonephritis	Left Gordon
6	F	W	L		Lobar pneumonia	Left Gordon
58	F	W	L		Coronary thrombosis; diabetes	Left knee jerk greater than right; left abdominals diminished
50	F	W	R		Acute bronchitis	Bilateral Babinski; left Rossolimo
43	F	W	R		Peritonsillar abscess	Right Gordon
33	F	W	R		Cystic ovary	Right Babinski; right abdominals diminished
44	F	W	L		Lobar pneumonia	On testing for right Gordon, left Gordon noted abdominals barely obtained
58	F	W		+	Diabetes	Absent abdominals
63	M	W	R		Aortic aneurysm	Right Rossolimo; unequal, sluggish pupils
21	F	W	R		Incomplete abortion	Abdominals very sluggish
48	M	W	L		Rheumatic heart disease	Left Gordon; right Babinski
64	F	W	R		Insulin shock	Right Gordon
47	M	W		+	Peptic ulcer	Bilateral Gordon
57	M	W		+	Acute coronary thrombosis	Left knee jerk greater than right; abdominals absent
22	F	W	R		Incomplete abortion	Right Babinski
51	F	W	L		Diabetes	Left Gordon
65	M	W	L		Cirrhosis of liver	Left Gordon; absent abdominals
67	M	W		+	Cancer of mouth	Bilateral Gordon; left Babinski; bilateral Chaddock, absent abdominals
79	F	W	R		Cancer of colon	Left Babinski; absent abdominals
48	F	W	L		Bronchopneumonia	Bilateral Babinski; absent abdominals
75	F	W	L		Arteriosclerotic heart disease	Absent abdominals
58	M	W	R		Cirrhosis of liver	Right Babinski
68	M	W	L		Coronary sclerosis	Left Gordon; absent lower abdominals
67	F	W	L		Toxic thyroid	Absent abdominals
60	F	W		+	Hypertensive heart disease	Bilateral Gordon; right Babinski; right Hoffmann
68	F	W	R		Hypertensive heart disease	Absent abdominals
20	F	W		+	Acute gonorrheal salpingitis	Bilateral Gordon; bilateral Babinski
53	M	W	L		Aortic aneurysm	Reflexes hyperactive; pupils irregular, do not react to light

TABLE 2.—*Incidence of Oppenheim Sign in 2500 Cases Without Other Evidences of Nervous System Disease*

Age, yr.	Sex	Race	Unilat.	Bilat.	Diagnosis
22	F	B	L		Rheumatic heart disease
37	F	W	R		Rheumatic heart disease
23	F	W	R		Incomplete abortion
59	F	W	L		Hypertensive heart disease
35	F	B	R		Acute bronchitis
26	F	W	R		Incomplete abortion
75	M	W	L		Peptic ulcer
15	F	W	R		Acute appendicitis
22	F	W	R		Incomplete abortion
65	M	W	R		Hypertensive heart disease
51	F	W	R		Cancer of breast
60	M	W	R		Cancer of bowel
43	F	W	R		Diabetes mellitus
33	F	W	L		Cystic ovary
66	F	W	L		Reticular-cell sarcoma of lymph node
49	F	W	R		Chronic cholecystitis
60	F	W		+	Hypertensive heart disease
40	F	W	L		Hypertensive heart disease
6	M	B	R		Rheumatic fever

TABLE 3.—*Summary of Tables 1 and 2*

	Total No. of Cases	Bilateral Oppenheim Sign	Unilateral Oppenheim Sign	
			Right	Left
With other evidences of nervous system disease	36	8	13	15
Without other evidences of nervous system disease	19	1	12	6

which doubtful responses of the big toe occur with the Babinski test.

GROUP 2.—In the inductee group seven had Oppenheim signs, an incidence of 1.00%. Of the seven with the Oppenheim sign, three had no other signs of lesions within the nervous system. Of the four with other signs of lesions within the nervous system, one had a Rossolimo sign on the opposite side and easily exhaustible abdominal reflexes, one had generalized hyperreflexia, one had diminished lower abdominal reflexes, and one had Babinski and Rossolimo

TABLE 4.—*Incidence of the Oppenheim Sign with Age*

Age Group, Yr.	0-19	20-39	40-59	60 and Over
Total no. in group	455	1015	705	325
No. with Oppenheim sign	3	13	21	18
Incidence of Oppenheim sign, %	0.66	1.28	2.97	5.54

signs on the opposite side. The Oppenheim signs in this group were all unilateral. There were 10 Oppenheim signs in the 781 patients between the ages of 21 and 35 of Group 1, giving an incidence of 1.28%, quite comparable to the 1.00% of the inductees.

Summary and Conclusions

The incidence of the Oppenheim sign was investigated in two control groups: Group 1, consisting of 2500 non-neurologic admissions to a general hospital, and Group 2, of 706 inductees between the ages of 21 and 35.

The incidence of this sign was 2.20% in the 2500 non-neurologic admissions and 1.00% in the inductee group.

The Oppenheim sign increases in frequency with rise in age. Sex and race show no significant differences.

Since it occurred with other signs of lesions within the nervous system in 65.5% of the 55 patients who showed the sign in the non-neurologic admissions, the presence of the Oppenheim sign is in favor of disease of the nervous system, the involvement being either interference with or actual lesion of the pyramidal tract.

REFERENCES

1. Oppenheim, H.: Zur Pathologie der Hautreflexe an den unteren Extremitäten, Monatsschr. Psychiat. u. Neurol. 12:518, 1902.

2. Pfeifer, B.: Beitrag zur klinischen Bedeutung des Babinski'scher Fusssohlenreflexes und des Oppenheim'schen Unterschenkelreflexes, Monatsschr. Psychiat. u. Neurol. 14:270, 1903.

3. Cassirer, R.: Über den Oppenheim'schen Unterschenkelreflex, Monatsschr. Psychiat. u. Neurol. 14:37, 1903.

4. Schlesinger, H.: Sie Sehnen- und Hautreflexe an den unteren Extremitäten bei alten Leuten, Deutsche Ztschr. Nervenh. 47-48:710, 1913.

5. Deutsch, J.: Über Grosszehen-Phänomene bei gesunden ältern Kindern, Ann. pædiat. 164: 273, 1945.

6. Zhukovski, M. W.: Plantar Toe Flexion Phenomenon, Obozr. psikhiat. nevrol. 15:200, 1910.

7. Myerson, A.: Note on Contralateral Oppenheim and Gordon Reflexes, with Observation in 2 Cases, J. Nerv. & Ment. Dis. 40:574, 1913.

8. Piotrowski, A.: Über einen neuen antagonistischen Reflex, Berl. klin. Wchnschr. 50:726, 1913.

9. Gordon, A.: A Propos of the Contralateral Oppenheim and Gordon Reflexes, J. Nerv. & Ment. Dis. 41:164, 1914.

10. Lewitsky, A.: Die diagnostische Bedeutung des Reflexes der kleinen Zehe (Prof. Puussepp' schen Reflex), Folia neuropath. eston. 3-4:386, 1925.

11. Rouquier, A.-J.-A.: La Recherche correcte des réflexes tendineux et cutanés, Arch. méd. et pharm. mil. 80:566, 1924.

12. Zanuttini, P.: Brevi Note e ricerche riguardanti il segno di Babinski e quello di Oppenheim, Gior. med. mil. 62:821, 1914.

13. Nielsen, J. M.: A Textbook of Clinical Neurology, Ed. 3, New York, Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1951, p. 89.

14. Purves-Stewart, J.: The Diagnosis of Nervous Diseases, Ed. 9, Baltimore, The Williams & Wilkins Company, 1945, p. 544.

15. Wechsler, I. S.: A Textbook of Clinical Neurology, Ed. 6, Philadelphia, W. B. Saunders Company, 1947, p. 20.

16. Monrad-Krohn, G. H.: The Clinical Examination of the Nervous System, Ed. 8, New York, Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1947, p. 173.

17. Brain, W. R.: Diseases of the Nervous System, Ed. 3, New York, Oxford University Press, 1947, p. 42.

18. Alpers, B. J.: Clinical Neurology Philadelphia, F. A. Davis Company, 1946, p. 52.

19. Fulton, J. F.: Physiology of the Nervous System, Ed. 3, New York, Oxford University Press, 1949, p. 411.

20. Walshe, F. M. R.: Diseases of the Nervous System, Ed. 8, Baltimore, The Williams & Wilkins Company, 1955, p. 22.

21. Lassek, A. M.: The Pyramidal Tract, Springfield, Charles C Thomas, Publisher, 1954, pp. 9, 50.

22. DeJong, R. N., in Clinical Neurology, edited by A. B. Baker, New York, Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1955, Vol. 1, p. 72.

23. Savitsky, N., and Madonick, M. J.: Statistical Control Studies in Neurology: I. The Babinski Sign, Arch. Neurol. & Psychiat. 49:272, 1943.

24. Madonick, M. J.: Statistical Control Studies in Neurology: III. The Hoffmann Sign, A.M.A. Arch. Neurol. & Psychiat. 68:109, 1952.

25. Madonick, M. J., and Savitsky, N.: Statistical Control Studies in Neurology: V. The Rossolimo Sign, A. M. A. Arch. Neurol. & Psychiat. 72:365, 1954.

26. Nathan, P. W., and Smith, M. C.: The Babinski Response: A Review and New Observations, J. Neurol. Neurosurg. & Psychiat. 18: 250, 1955.

27. Ganfini, G.: Il Rinforzo del fenomeno di Babinski (nota di tecnica semeiologica) Riv. sper. freniat. 60:80, 1936.

Effects of Methyl Alcohol on Cerebral Blood Flow and Metabolism

Observations During and After Acute Intoxication

LOUIS L. BATTEY, M.D., Augusta, Ga.
JOHN L. PATTERSON Jr., M.D., Richmond, Va.
and
ALBERT HEYMAN, M.D., Durham, N. C.

Methyl alcohol and its toxic metabolic products exert their severest and most destructive effects upon the structure and function of nerve tissue. Depression or derangement of cerebral function is present to some degree in almost every patient with methanol intoxication, with symptoms ranging from headache and confusion to profound coma.* Impairment of optic nerve function is also commonly found, manifested by disturbances varying from transient amblyopia to permanent and total blindness.

Heretofore, observations on the physiological abnormalities produced in the brain by methyl alcohol have been limited to studies on experimental animals. The 1951 outbreak of methanol poisoning in Atlanta provided an opportunity for the measurement of the cerebral blood flow and oxygen consumption in several of these patients. This paper reports the findings in five cases during or soon after the acute phase of the disorder and includes follow-up studies on four of these persons.

Recorded for publication Feb. 23, 1956.

Supported in part by Contract N9onr92500, Office of Naval Research, and in part by a grant from the National Institutes of Health, U. S. Public Health Service.

From the Departments of Physiology and Medicine, Emory University School of Medicine, and Medical Service of Grady Memorial Hospital, Atlanta. Present addresses: 1407 Gwinnett St., Augusta, Ga. (Dr. Battey); Department of Medicine, Medical College of Virginia, Richmond, Va. (Dr. Patterson); Department of Neurology, Duke University School of Medicine, Durham, N. C. (Dr. Heyman).

*References 1 and 2.

Material and Methods

Full details of the outbreak of poisoning have been reported elsewhere by Cooper and associates,[2] and only a brief description is given here. During the week beginning Oct. 21, 1951, a total of 323 patients who had ingested bootleg whisky were seen at Grady Memorial Hospital. Analysis of samples of this concoction showed 35% to 40% methyl alcohol by weight and 2% to 4.5% ethyl alcohol. Patients in acute intoxication exhibited variations of the characteristic clinical picture, with depressed sensorium, delirium, loss of consciousness, and visual disturbances. Severe abdominal pain, vomiting, dyspnea, and headache were among the most prominent symptoms. A fatal result followed the reported ingestion of as little as 1 oz. (30 cc.) of the mixture, while another patient survived the ingestion of 1 pt. (500 cc.). There were 41 deaths. The deaths which occurred while the patient was under observation appeared to be respiratory in nature, with cardiac activity persisting after cessation of respiration.

Four of the five patients subjected to cerebral studies were below 40 years of age, and the fifth was 63 years old. Three of the group had a history of moderate hypertension. They had ingested from 1 oz. to 1 pt. of the contaminated whisky. On admission to the hospital, four of the subjects were stuporous and irrational, and one was comatose. Initial studies were done within two days following the onset of symptoms, at which time the sensorium was clear in four of the patients. Coma persisted in the fifth patient, who died four days after the initial cerebral blood flow measurement. All had received sodium bicarbonate, most of it intravenously, prior to the initial studies. The dose of the alkali averaged 70 gm. in the four patients who survived; 140 gm. in two days was given to the patient who died (Case 5). Case 5 also received corticotropin by intravenous drip. Acidosis, as suggested by reduced arterial CO_2, was still present in two patients.

Each of the five patients had marked visual impairment on admission. Three of them showed impairment in visual acuity at the time of the initial blood flow procedure. One patient had total loss of vision, which persisted throughout his hospitalization.

Follow-up studies were done approximately one week later on the four surviving patients, at which time the acidosis had subsided and mental changes had improved. Ophthalmoscopic evidence of optic nerve damage and retinal edema had diminished, but visual impairment was still present in every patient.

The cerebral blood flow (CBF) was studied by the nitrous oxide method of Kety and Schmidt [3] with the slight modifications previously described.[4]

The cerebral oxygen consumption (CMR_2) was obtained from the CBF multiplied by the arteriovenous oxygen difference. The cerebral vascular resistance was obtained from the mean arterial pressure, measured with a damped mercury manometer, divided by the cerebral blood flow. The blood oxygen and carbon dioxide were determined by the combined procedure for the analysis of both gases on a single sample, as described by Peters and Van Slyke.[5]

Results

The individual and mean values for the cerebral functions measured during acute methanol intoxication and a week later, in convalescence, are given in the accompanying Table. These are compared with mean values obtained from a group of 15 normal subjects of comparable mean age and age distribution. Three of these control subjects were between the ages of 60 and 65; the remainder were less than 45 years of age. Values for statistical significance are given, although it is realized that the number of patients is small for this type of analysis.

Cerebral blood flow was decreased appreciably in each patient during the stage of acute intoxication and ranged from 30 to 42 cc/100 gm. brain/min. The mean value of 35 cc. was 30% below the normal mean of 50 cc/100 gm/min. One week later there was increase in flow in two of the four surviving patients, amounting to 8 and 15 cc/100 gm/min. in Cases 2 and 1, respectively. However, the mean value still remained 14% below normal. This decrease in blood flow was associated with a rise in cerebral vascular resistance. The CVR in each patient was above the normal mean of 1.8 mm. Hg/cc. blood flow/100 gm. brain/min. The mean of the group was 72% greater than normal. Following treatment, the CVR showed an appreciable fall in only one of the four surviving patients. Mean arterial blood pressures were slightly lower during the stage of acute intoxication than during convalescence.

The oxygen utilization of the brain ($CMRO_2$) was markedly decreased in each patient during acute intoxication, the average for the group being 30% below the control value of 3.0 cc/100 gm. brain/min. During convalescence the cerebral oxygen consumption increased markedly in two patients and very slightly in the other two patients. The mean value still remained 13% below normal.

The arterial CO_2 content during acute intoxication was greatly reduced. Unfortunately, pH determinations could not be obtained, so that values for arterial CO_2 tension could not be calculated. Values for hemoglobin and hematocrit were increased in all cases during acute intoxication, probably as a result of dehydration. Mean values for arterial oxygen saturation were slightly below control values during intoxication and were little changed at the time of the follow-up procedure.

Clinical examination six months after intoxication revealed complete blindness with bilateral optic trophy in one patient (Case 3) and marked loss of vision in two other patients (Cases 1 and 4). No other sequalae were noted. One patient (Case 2) did not return for further study. Repeat physiological studies in Case 3 showed continued depression of cerebral oxygen consumption, with values of 2.5 cc/100 gm/min. three weeks and, again, eight months after the intoxication. The

Case	Sex	CBF Cc./100 Gm./Min.		$CMRO_2$ Cc./100 Gm./Min.		CVR Mm.Hg/ Cc./100 Gm./Min.		$(A\text{-}V)O_2$ Mm. Hg		Mean Art. Pressure Mm. Hg		H'crit, %		Hgb Gm./100 Cc.	Art. CO_2 mM/Liter		Cerebral R.Q.		Approx. Amt. Methanol Ingested	Ven. CO_2 (on Adm.) mM/Liter	Clinical Status*		
		I†	II†	I	II	I	II	I	II	I	II	I	II		I	II	I	II			Admission	I	II
1 34	F	35	50	1.4	2.4	3.1	2.2	3.9	4.9	109	111	41	34	12.3	19.7	20.2	0.89	0.80	½ pt.	9	D,R,N, V4+,A	Alert,O, V+	Alert,O,P, N,V+
2 26	M	38	41	1.8	2.5	2.6	2.4	4.7	6.1	99	97	48	38	16.1	13.9	22.4	0.74	0.66	1 oz.	13	L,D,R,N, V4+,A	Alert,R,N, V2+,A	Alert,O,R, V3+
3 40	M	30	38	2.6	2.8	3.8	3.9	8.7	7.4	115	147	41	39	13.0	4.9	22.9	0.85	0.86	½ pt.	15	D,R,N, V4+	O,L,R,N, V4+	Alert,P,R, N,V4+
4 37	M	42	42	2.3	2.5	1.9	2.4	5.5	5.9	80	100	41	34	14.7	17.9	24.2	0.99	0.77	2 oz.	4.5	L,R,N, V4+,A	L,N,V2+, A	Alert,N, V2+
5 63	F	31	....	2.2	....	3.9	....	7.1	....	120	....	40	..	12.6	25.6	....	0.93	..	½ pt.	8	C,R,N,A, Hk; did not respond	C,R,N	Died 4th day after Procedure I‡
Mean of first four		36	43	2.0	2.6§	2.9	2.7	5.7	6.1	101	114	43	36	14.0	14.1	22.4	0.87	0.77					
Mean of five		35‖	....	2.1‖	....	3.1‖	....	6.0	....	105¶	....	42	..	13.7	16.4	....	0.88	..					
Mean of controls		50	....	3.0	....	1.8	....	6.1	....	89	....	39	..	11.3									

* Clinical status: O=oriented; L, lethargic; D, disoriented; C, comatose; P, pupillary changes; R, retinal edema; N, optic nerve changes; V, visual defect (1+, 2+, 3+, 4+); A, acidosis; Hk, hypokalemia.

† I, on admission; II, follow-up.

‡ Autopsy findings: Cerebral edema and congestion; pulmonary edema, mild; acute necrosis of pancreas; congestion of G. I. tract, liver, and kidneys.

§ Significance of difference from mean of procedure I=$0.1 > P > 0.05$.

‖ Significantly different ($P<0.01$) from mean in 15 control subjects of the same age range.

¶ $P<0.05$.

cerebral blood flow was slightly increased at eight months, the value being 41 cc/100 gm/min.

Comment

An interesting feature of the results was the failure of the cerebral oxygen consumption during the acute stage of methanol intoxication to correlate well with the existing clinical picture or with the prognosis of the individual patient. The two patients with the lowest values for cerebral metabolism (Cases 1 and 2) had only slight mental changes and survived. The comatose patient (Case 5), who later died, had a somewhat higher value for cerebral metabolism. Similar lack of correlation between the $CMRO_2$ and the mental state has also been found in uremia,[6] the explanation for which is not clear in either case.

Several factors may be responsible for the observed increase in cerebral vascular resistance following methanol ingestion, the most important of which would seem to be cerebral edema. Varying degrees of cerebral edema and hyperemia were found in all the autopsied cases of the Atlanta mass poisoning. This marked interstitial edema of the brain, combined with arterial and capillary damage with resultant swelling, would doubtless produce a diminution in the caliber of the vascular bed and a consequent reduction in cerebral blood flow.

Although the pH of the blood could not be measured in these patients, there is little doubt that it was reduced, at least in the patients with lowered blood CO_2 content. At the present time the effect of changes in pH on cerebral blood flow are the subject of controversy. Kety and his associates[7] believed that a decrease in pH was responsible for the increased blood flow observed in their cases of diabetic acidosis. However, recent studies by Schieve and Wilson[8] and observations on 10 subjects in this laboratory † have shown that cerebral blood flow is either reduced or not affected by the acidosis induced by intravenous administration of ammonium chloride. On the basis of his observations, Schieve suggested that regulation of cerebral blood flow is more closely dependent on CO_2 tension than on pH. Acidosis, as suggested by a definitely reduced blood CO_2 content, while present in all of our patients on admission, existed in only two of them during the initial blood flow determinations and was absent a week later, at the time of follow-up studies. It appears doubtful, therefore, that change in pH was an important factor in the reduction in cerebral blood flow observed in our series.

It is reasonable to assume that the arterial CO_2 tension, at least in the patients with low blood CO_2 content, was reduced below normal. The acidosis would bring about a conversion of blood bicarbonate to carbonic acid. Hyperventilation under the stimulus of the acidemia would be expected to continue until the arterial pCO_2 was reduced below normal, and the ratio of dissolved to bound CO_2 in the plasma returned toward normal. A primary reduction in arterial pCO_2 has been shown to be a cerebral vasoconstrictor stimulus.[9] In diabetic acidosis arterial pCO_2 is markedly reduced; yet for some reason blood flow is only slightly reduced in the milder cases and is actually increased in coma.[7]

The very significant decrease in cerebral oxygen consumption found in acute methanol poisoning is in keeping with certain earlier observations. Leaf and Zatman[10] reported that formaldehyde and formate, both of which are metabolic products of methanol, depress the metabolism of ox retina, but that methanol itself is without effect. Roe[11] has stated that formic acid inhibits cell respiration by binding the ferment iron in the cells and that this reaction is increased in the

† Patterson, J. L., Jr., and Heyman, A.: Unpublished observations.

presence of acidosis. Gradinesco[12] demonstrated that methanol first causes excitability and then diminution in nerve response, resulting eventually in complete absence of nerve function. Additional observations on the toxic properties of methanol are reviewed by Bennett and colleagues.[13]

Our studies confirm the hypothesis that the oxidative processes of cerebral cells are impaired in acute methanol intoxication. It appears unlikely that the reduction in cerebral blood flow alone could account for this decrease in metabolism, since both functions were reduced to the same degree. The normal brain tolerates a 21% reduction in blood flow, for a short time at least, without depression of metabolism.[14] A significant decrease in arterial oxygen content was not found in any of our patients and therefore was not instrumental in reducing the oxygen utilization by the brain. Rather, it would seem to have resulted from some more direct action of the toxic by-products of methanol, foremost of which is formic acid, and presumably also formaldehyde.

Summary

1. In five patients with acute methanol intoxication, both the mean cerebral blood flow and the oxygen consumption were reduced 30% below the normal values. One week later, these functions in four surviving patients were only 14% below normal.

2. The degree of depression of cerebral metabolism correlated poorly with the reported amount of methanol ingested. The patient who died had a higher initial level of cerebral oxygen consumption than did two patients who survived.

Misses Mary Ruth Fordham, Mary Bell, and Mary Upshaw, and Mrs. Louise Thompson gave technical assistance.

REFERENCES

1. Keeney, A. H., and Mellinkoff, S. M.: Methyl Alcohol Poisoning, Ann. Int. Med. 34:331, 1951.

2. Cooper, M. N.; Mitchell, G. L.; Bennett, I. L., Jr., and Cary, F. H.: Methyl Alcohol Poisoning: An Account of the 1951 Atlanta Epidemic, J. M. A. Georgia 41:48, 1952.

3. Kety, S. S., and Schmidt, C. F.: The Nitrous Oxide Method for the Quantitative Determination of Cerebral Blood Flow in Man: Theory, Procedure and Normal Values, J. Clin. Invest. 27:476, 1948.

4. Patterson, J. L., Jr.; Heyman, A., and Nichols, F. T.: Cerebral Blood Flow and Oxygen Consumption in Neurosyphilis, J. Clin. Invest. 29: 1327, 1950.

5. Peters, J. P., and Van Slyke, D.D.: Quantitative Clinical Chemistry, Vol. II: Methods, Baltimore, Williams & Wilkins Company, 1932.

6. Heyman, A.; Patterson, J. L., Jr., and Jones, R. W., Jr.; Cerebral Circulation and Metabolism in Uremia, Circulation 3:558, 1951.

7. Kety, S. S.; Polis, B. D.; Nadler, C. S., and Schmidt, C. F.: The Blood Flow and Oxygen Consumption of the Human Brain in Diabetic Acidosis and Coma, J. Clin. Invest. 27:500, 1948.

8. Schieve, J. F., and Wilson, P.: The Changes in Cerebral Vascular Resistance of Man in Experimental Alkalosis and Acidosis, J. Clin. Invest. 32:33, 1953.

9. Kety, S. S., and Schmidt, C. F.: The Effects of Active and Passive Hyperventilation on Cerebral Blood Flow, Cerebral Oxygen Consumption, Cardiac Output, and Blood Pressure of Normal Young Men, J. Clin. Invest. 25:107, 1946.

10. Leaf, G., and Zatman, L. J.: A Study of the Conditions Under Which Methanol May Exert a Toxic Hazard in Industry, Brit. J. Indust. Med. 9:19, 1952.

11. Roe, O.: The Roles of Alkaline Salts and Ethyl Alcohol in the Treatment of Methanol Poisonings, Quart. J. Stud. Alcohol 11:107, 1950.

12. Gradinesco, A., and Degan, C.: L'action de alcools méthylique et éthylique sur l'excitabilité du nerf. Détermination faite par la méthode du la chronaxie, J, physiol. et path. gén. 32:826, 1934.

13. Bennett, I. L., Jr.; Cary, F. H.; Mitchell, G. L., Jr., and Cooper, M. N.: Acute Methyl Alcohol Poisoning: A Review Based on Experiences in an Outbreak of 323 Cases, Medicine 32:431, 1953.

14. Scheinberg, P., and Stead, E. A., Jr.: The Cerebral Blood Flow in Male Subjects as Measured by the Nitrous Oxide Technique: Normal Values for Blood Flow, Oxygen Utilization, Glucose Utilization, and Peripheral Resistance, with Observations on the Effect of Tilting and Anxiety, J. Clin. Invest. 28:1163, 1949.

Chlorpromazine and Reserpine

(A) Effects of Each and of Combinations of Each with Morphine
(B) Failure of Each in Treatment of Abstinence from Morphine

H. F. FRASER, M.D.
and
HARRIS ISBELL, M.D., Lexington, Ky.

It has been reported that chlorpromazine decreases the amount of narcotics required for the relief of pain (Laborit, Forster,[2] and Sadove[3] and their associates). On the other hand, Houde and Wallenstein[4] observed that there was no potentiation of the analgesic effect of morphine by chlorpromazine in the treatment of cancer patients. Several investigators have reported that chlorpromazine reduces the intensity of abstinence following the withdrawal of morphine or other opiate-like drugs from addicted persons (Stähelin and Kielholz[5]; Cummins and Friend[6]; Friedgood and Ripstein,[7] and Aivazian[8]). Carey[9] found that reserpine was more effective than a placebo in the treatment of opiate addicts who had been arrested and their narcotic drugs abruptly discontinued during incarceration.

Studies at the National Institute of Mental Health Addiction Research Center, Lexington, indicate that neither chlorpromazine nor reserpine is of value in treating acute abstinence from morphine. Since these findings are not in agreement with those of other investigators cited above, they are being reported. In addition, effects of single doses of morphine, reserpine, and chlorpromazine, and the effects of morphine combined with chlorpromazine and with reserpine will be presented.

Received for publication April 5, 1956.

From the National Institute of Mental Health Addiction Research Center, Public Health Service Hospital.

Method

In testing the effects of single doses of a placebo, of chlorpromazine, and of combinations of chlorpromazine with morphine, eight healthy male subjects who were former opiate addicts were used. Another group of eight similar subjects was used in testing the effect of single doses of a placebo, reserpine, morphine, and combinations of reserpine and morphine. Objective measurements included degree of miosis, respiratory minute volume, rectal temperature, respiratory and pulse rates, and blood pressure. In addition, evidence of morphine-like behavior and subjective reports of morphine-like "euphoria" were recorded. In testing any series of drugs, each subject received each drug in the series and thus served as his own control for all comparisons and for statistical treatment of data. The details of the methods have been fully described.*

In testing the efficacy of chlorpromazine and reserpine for relieving symptoms of abstinence from morphine, physically healthy male volunteers who were former opiate addicts were addicted and stabilized on 60 mg. of morphine sulfate given subcutaneously every six hours for at least three weeks. Morphine was abruptly replaced with placebo injections, and the intensity of abstinence during a test period of either 24 or 40 hours was measured according to the hourly-point method of Himmelsbach.[10] At the conclusion of the placebo injections the subjects were restabilized on the same dose of morphine sulfate. In another experiment, the patients were advised that the morphine was being replaced with another drug; actually, they were given their customary doses of morphine. Again, the intensity of abstinence was recorded, providing a positive control. The patients were then continued on morphine. After one or two weeks, morphine was discontinued, chlorpromazine or reserpine was administered, and the intensity of abstinence was measured again.

The specific doses and routes of administration

* References 10 and 11.

of each drug and placebo and the number of subjects in each test will be described subsequently.

Results

Effects of Single Doses of Chlorpromazine Orally and Intramuscularly, Morphine Subcutaneously, and a Combination of Morphine and Chlorpromazine.—Chlorpromazine was administered orally in a dose of 50 mg., and intramuscularly in a dose of 25 mg., and the potentiating effect of both doses of chlorpromazine on morphine was tested, using both 10 and 30 mg. of morphine sulfate given subcutaneously.

Chlorpromazine alone, either orally or intramuscularly, produced a feeling of lethargy associated with drowsiness. None of the eight subjects liked the effects. Patients developed a mild pallor and were less active. Pupillary diameter (Fig. 1), respiratory minute volume (Fig. 1), rectal temperature, respiratory and pulse rates, and recumbent blood pressure were not significantly altered by chlorpromazine.

The miotic effects of the chlorpromazine-morphine combinations were greater than those of morphine alone, but respiratory depression induced by morphine was not increased by the combination (Fig. 1). Many of the subjects reported that morphine-like "euphoria" persisted for as long as 10 to 15 hours after the combination, whereas normally this effect would have subsided within six to eight hours following morphine alone. Chlorpromazine did not alter the effect

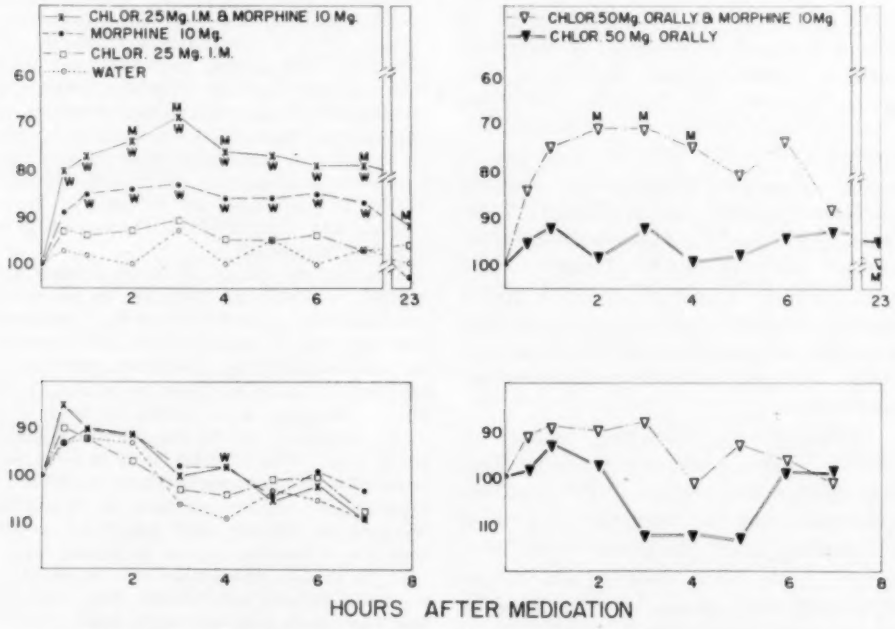


Fig. 1.—Effects on diameter of pupils and respiratory minute volume of morphine sulfate, 10 mg; chlorpromazine, 25 mg. intramuscularly; chlorpromazine, 50 mg. orally, and a placebo (water). These effects are compared with those of 10 mg. of morphine combined with chlorpromazine. Each point on each curve represents the mean results obtained on the same eight subjects. The letter *W* denotes a statistically significant difference of that value as compared with placebo. The letter *M* denotes a statistically significant difference between that point and an equivalent point for morphine sulfate.

A parallel series of experiments were carried out using 30 mg. of morphine alone and with various combinations of chlorpromazine. The results obtained were entirely analogous to those observed with 10 mg. of morphine.

of morphine on rectal temperature, respiratory and pulse rates, and blood pressure.

Efficacy of Chlorpromazine in Treatment of Acute Abstinence from Morphine.—Morphine was abruptly withdrawn from four patients who had been stabilized on 240 mg. of the drug daily, and chlorpromazine was substituted for the morphine in a total average dose during three separate tests, as follows: 550 mg. orally; 1600 mg. orally, and 275 mg. intramuscularly. Administration of chlorpromazine was begun six hours prior to discontinuing morphine and was continued at 6-hour intervals for 36 hours after the last dose of morphine. Figure 2 shows the intensity of abstinence under the various conditions, the routes of administration, and the dose of chlorpromazine given. It is obvious that a total oral dose of 550 mg. was of no benefit, and that increasing this total dose to 1600 mg. daily produced no significant decrease in the intensity of abstinence from morphine, even though symptoms and signs of chlorpromazine side-effects were present. Similarly, when chlorpromazine was given intramuscularly, no definite amelioration of abstinence occurred.

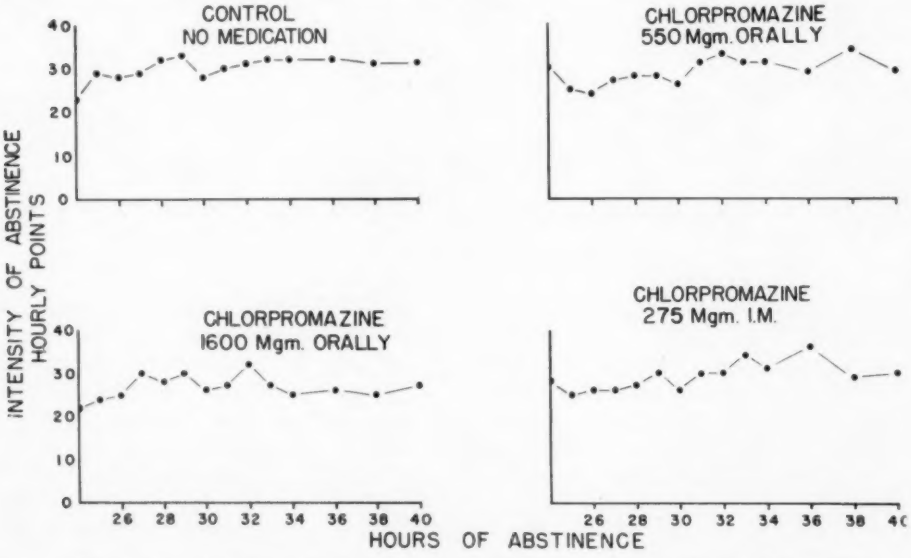


Fig. 2.—Intensity of abstinence from morphine when the drug was abruptly discontinued and no medication (a placebo) was given, as compared with the intensity of abstinence when morphine was abruptly discontinued and chlorpromazine substituted for the morphine. Each point on each curve represents the mean of results obtained on the same four subjects. Note that the intensity of abstinence is as great after chlorpromazine as after placebo.

Effects of Single Doses of Reserpine Orally, Morphine Subcutaneously, and a Combination of Morphine and Reserpine.—One milligram of reserpine orally produced no subjective or objective effects except a more restful sleep during the night following its administration.

One milligram of reserpine or a reserpine placebo was administered orally, and concurrently 30 mg. of morphine was injected subcutaneously. Reserpine-morphine combinations induced miotic effects similar to those of morphine alone (Fig. 3). Several observations of minute volume suggest that reserpine antagonized slightly the depressant effects of morphine; however, none of the differences illustrated (Fig. 3) are statistically significant.

Concurrent Administration of Reserpine and Morphine in Addicted Patients.—Eight patients addicted to 240 mg. of mor-

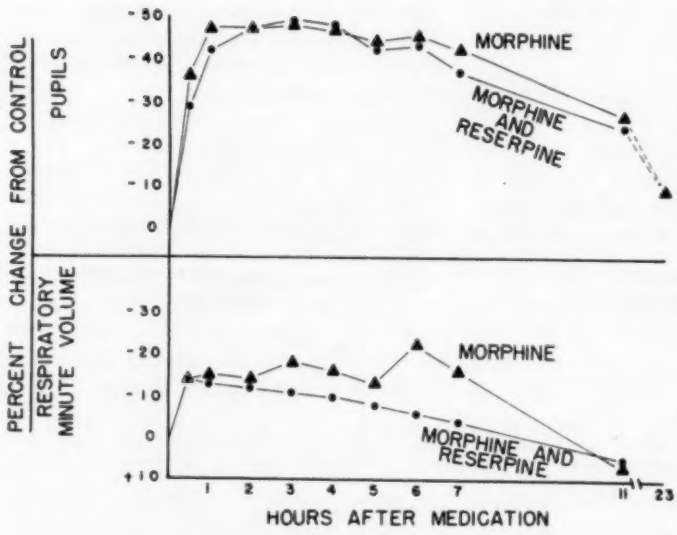


Fig. 3.—Effects of 30 mg. of morphine sulfate subcutaneously on diameter of pupils and respiratory minute volume, as compared with the effects of 30 mg. of morphine sulfate subcutaneously plus 1 mg. of reserpine orally. Each point on each curve represents the mean of results obtained on the same eight subjects. Each of these eight subjects was also given a placebo (water), and, in another test, 1 mg. of reserpine orally. Since the curves obtained for a placebo and for reserpine were entirely similar, they are not illustrated.

phine daily received 1 mg. of reserpine orally and their regular dose of morphine (60 mg.) at 10 a.m. This dose of reserpine and morphine was repeated at 4 p.m. Symptoms of nausea, stuffiness of the nose, headache, injected conjunctiva, and flushing of the face developed in all patients one and one-half hours after the second dose of reserpine. Two patients vomited, and two were disturbed by a sensation that they "couldn't get their breath." All of these patients disliked the sensation of morphine plus reserpine, while addicted. This experiment, as well as another one performed on the same subjects, indicates that in patients addicted to morphine the side-reactions of reserpine seem to be intensified.

Efficacy of Reserpine in Treatment of Acute Abstinence from Morphine.—This was tested in eight subjects addicted to 240 mg. of morphine daily. Reserpine was given intramuscularly in successive doses of 3,

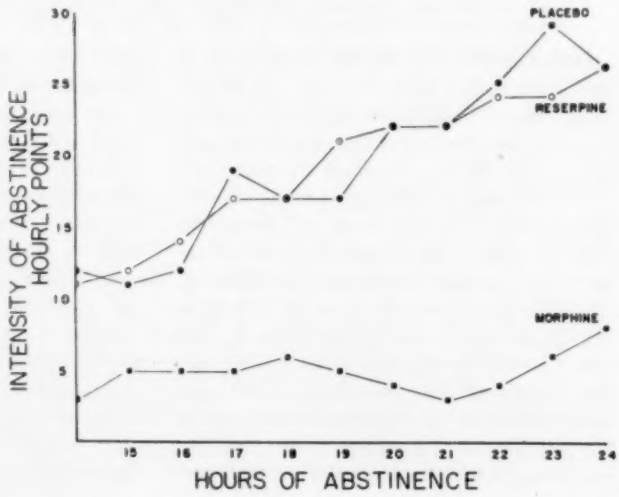


Fig. 4.—Intensity of abstinence from morphine when abruptly discontinued and a placebo was substituted, or when reserpine was substituted, or when morphine was continued (positive control). Note that the intensity of abstinence is as great after reserpine as after placebo.

5, and 2 mg. when the patients had been 6, 14, and 18 hours abstinent from morphine. Reserpine was of no value in the treatment of acute abstinence from morphine, since the intensity of abstinence was no less when reserpine was administered than when a placebo was given (Fig. 4). Furthermore, all subjects complained that the medication was worse than no treatment, and one patient refused to cooperate and take all the doses of reserpine during withdrawal.

In another experiment, using the same eight subjects, reserpine was tested orally in a total dose of 2 mg. for its ability to relieve abstinence. Again, the intensity of abstinence was practically identical to that obtained when a placebo was administered, and none of the patients were subjectively improved.

Comment

The failure of chlorpromazine and reserpine in the treatment of acute abstinence from morphine as herein described is not in agreement with the results reported by other investigators. However, proper evaluation of new drugs for the treatment of abstinence from opiates requires stabilized opiate intoxication for each subject and preliminary placebo withdrawals prior to testing the unknown for its efficacy in the treatment of abstinence. Such procedures were not followed by those reporting favorably on chlorpromazine and reserpine. It is essential also that the environment be strictly controlled so that contraband narcotics cannot be introduced into the experimental situation. The latter requirement is not feasible in an ordinary general or mental disease hospital.

Abstinence from opiates is not a dangerous condition insofar as the life of the patient is concerned. Substitution of methadone orally for the opiate the patient is using, and then gradually reducing the dose of methadone over a period of 3 to 10 days, is simple yet effective therapy, which carries no risk. Since neither chlorpromazine nor reserpine is effective in suppressing symptoms of abstinence, and since the use of either might conceivably add to the negligible risk of the standard treatment, neither drug should be used during the acute phase of abstinence from opiates.

The failure of chlorpromazine and reserpine in the treatment of acute abstinence from morphine does not mean that these drugs would not be useful after withdrawal of opiates has been completed. During this recovery phase, addicts, though showing none of the objective manifestations of abstinence, complain bitterly of insomnia, nervousness, etc., and in this situation reserpine or chlorpromazine might be useful. Furthermore, since the drugs may be useful in the symptomatic treatment of the personality disorders associated with addiction, they might be of value in preventing relapse to narcotics. Neither of these possible uses in the postwithdrawal treatment of addiction has been evaluated properly.

Summary

In nontolerant former opiate addicts, chlorpromazine enhanced the miotic effects of morphine and prolonged some of the subjective effects. One milligram of reserpine given orally and concurrently with 30 mg. of morphine subcutaneously did not increase the effects of morphine.

In patients addicted to morphine, neither chlorpromazine nor reserpine administered orally or intramuscularly reduced the intensity of abstinence from morphine.

REFERENCES

1. Laborit, H.; Jaulmes, C., and Benitte, A.: Certain Experimental Aspects of Artificial Hibernation, Anesth. et analg. 9:232-239, 1952.

2. Forster, S.; Forster, E.; Maier, A., and Blum, H.: Potentialized Anesthesia in Thoracic Surgery, Anesth. et analg. 9:250-260, 1952.

3. Sadove, M. S.; Levin, M. J.; Rose, R. F.; Schwartz, L., and Witt, F. W.: Chlorpromazine and Narcotics in the Management of Pain of Malignant Lesions, J.A.M.A. 155:626-629, 1954.

4. Houde, R. W., and Wallenstein, S. L.: Analgetic Power of Chlorpromazine Alone and in Combination with Morphine, Fed. Proc. 14:1, 1955.

5. Stähelin, J. E., and Kielholz, P.: Largactil, ein neues vegetatives Dämpfungsmittel bei psychischen Störungen, Schweiz. med. Wchnschr. 83: 581-586, 1953.

6. Cummins, J. F., and Friend, D. G.: Use of Chlorpromazine in Chronic Alcoholics, Am. J. M. Sc. 227:561-564, 1954.

7. Friedgood, C. E., and Ripstein, C. B.: Use of Chlorpromazine in the Withdrawal of Addicting Drugs, New England J. Med. 252:230-233, 1955.

8. Aivazian, G. H.: Chlorpromazine in the Withdrawal of Habit Forming Drugs in Addicts, Dis. Nerv. System 16:1-4, 1955.

9. Carey. E. F.: A New Approach to the Emergency Treatment of Sickness Caused by Narcotic Withdrawal, Ann. New York Acad. Sc. 61: 222-229, 1955.

10. Fraser, H. F.; Nash, T. L.; Van Horn, G. D., and Isbell, H.: Use of Miotic Effect in Evaluating Analgesic Drugs in Man, Arch. internat. pharmacodyn. 98:443-451, 1954.

11. Isbell, H., and Fraser, H. F.: Actions and Addiction Liabilities of Dromoran Derivatives in Man, J. Pharmacol. & Exper. Therap. 107:524-530, 1953.

12. Himmelsbach, C. K.: Studies of Certain Addiction Characteristics of (*a*) Dihydromorphine ("Paramorphan"), (*b*) Dihydrodesoxymorphine-D ("Desomorphine"), (*c*) Dihydrodesoxycodeine-D ("Desocodeine"), and (*d*) Methyldihydromorphinone ("Metopon"), J. Pharmacol. & Exper. Therap. 67:239-249, 1939.

Correspondence

PROCAINE OIL BLOCKING OF GLOBUS PALLIDUS

To the Editor:—In the article by H. Narabayashi, T. Okuma, and S. Shikiba entitled "Procaine Oil Blocking of the Globus Pallidus," published in the January, 1956, issue of the ARCHIVES, pages 36-48, the authors discuss at great length the history of Parkinson's disease and quote numerous authors who performed cortical operations in extrapyramidal disorders. They then report the "conception of blocking of the globus pallidus." "The procedure was based on the idea of the antagonistic functional correlation of corpus striatum and the globus pallidus." They quote animal experiments by Wilson and Mettler and Ades in which the globus pallidus was stimulated and Meyer's operation on the caudate nucleus. They "thought that much more selective invasion of the caudate nucleus would be possible with the stereotactic method than by such a major neurosurgical procedure." In this way they try to create the impression that they were the first who performed stereotactic operations on the basal ganglia, not even mentioning with a single word the fact that we have reported such operations repeatedly since 1949. They also describe a stereoencephalotome that is merely an imitation of our apparatus. We feel that their method of only listing our references among others that have hardly a bearing on their work, without mentioning that their methods are just imitations or modifications of ours (injection of procaine in oil instead of electrolysis) is entirely inappropriate and misleading.

E. A. SPIEGEL, M.D.
H. T. WYCIS, M.D.
Broad & Ontario Sts.
Philadelphia 40

To the Editor:—In answer to the letter of Drs. Spiegel and Wycis, we think it necessary to emphasize the following points:

1. Though our concern is not particularly with priorities, we invite attention to the fact that our report in the January, 1956, issue of the ARCHIVES is concerned especially with procaine oil blocking of the globus pallidus in Parkinsonian rigidity. This operation was first performed in May, 1952, and the first report was published in March, 1953, in the *Proceedings of the Japan Academy*. Drs. Spiegel and Wycis have done ansotomy in paralysis agitans since 1952, but they reported pallidotomy only in cases of choreic movement. We believe selective pallidal invasion in Parkinsonism is our innovation. This idea was reached by experienece with the same procedure in cases of double athetosis and was not suggested by their work.

In this connection, ligation of the anterior choroidal artery and injection of procaine or alcohol into the globus pallidus by Dr. I. Cooper, of New York, are to be noted.

2. We always have acknowledged the priority of Drs. Spiegel and Wycis in adapting the stereotactic instrument to humans, and in previous papers, published in Japan, due credit to them was given. It seems absurd to repeat this credit. But this does not mean our technique is an imitation of theirs. For instance, our instrument is superior in the points that it does not refer to the pineal body as the zero point and all operative procedure is performed with the patient in the supine position and with local anesthesia. Their method and ours are both modifications of the Horsley-Clarke technique, published in 1908, and these modifications make scientific progress.

3. At present, 96 pallidum operations for Parkinsonism have been done in our laboratory, and stereoencephalotomy is being studied and used in five medical schools and one specialized private hospital in this country. The problem at hand is the theoretical analysis of hyperkinesis.

H. NARABAYASHI, M. D.
Tokyo University School of Medicine
Tokyo, Japan

BIBLIOGRAPHY

Uchimura, Y., and Narabayashi, H.: Stereotaxic Apparatus, Psychiat. et neurol. jap., Vol. 52, 1951.

Narabayashi, H.: Stereotaxic Apparatus (Model II), Psychiat. et neurol. jap., Vol. 54, 1953.

———and Okuma, T.: Procaine Oil Blocking of the Globus Pallidus for Double Athetosis, Psychiat. et neurol. jap., Vol. 54, 1953.

Some Contemplations on the Role of Pallidum in Parkinsonism, Brain & Nerve 6:157, 1954.

Conceptions and Apparatus of the Stereotactic Operations, Brain & Nerve, Vol. 5, No. 6, 1953.

Procaine Oil Blocking of the Globus Pallidus for Treatment of Rigidity and Tremor of Parkinsonism: Preliminary Report, Proc. Japan. Acad. 29, No. 3, 1953.

———Okuma, T., and Shikiba, S.: Procaine Oil Blocking of the Globus Pallidus, A. M. A. Arch. Neurol. & Psychiat. 75:36, 1956.

Procaine Oil Blocking of the Globus Pallidus, Psychiat. et neurol. jap. 56:471, 1954.

Okuma, T.; Shimazono, Y.; Fukuda, T., and Narabayashi, H.: Cortical and Subcortical Recording in Nonanesthetized and Anesthetized Periods in Man, Electroencephalog. & Clin. Neurophysiol. 6:259, 1954.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND THE NEW YORK NEUROLOGICAL SOCIETY

JOSEPH W. OWEN, M.D., Chairman, Section on Neurology and Psychiatry, Presiding

Joint Meeting, Feb. 14, 1956

Metabolic Alterations Following Craniocerebral Trauma in the Human. DR. ALBERT W. COOK and DR. E. JEFFERSON BROWDER.

The manifold issues involved in any single instance of severe craniocerebral trauma are still not capable of resolution. Patients at times presenting similar clinical features may, on one hand, succumb; others survive with neurological deficit, and a few exhibit complete functional recovery. Evacuation of an intracranial clot in some may not favorably alter a downhill course; however, in other, seemingly comparable, situations a disastrous situation is completely reversed by appropriate surgery. Lesions observed post mortem may also fail to resolve all pertinent issues.

In view of the persistent unsatisfactory understanding of these problems, information was sought concerning metabolic alterations in patients with various degrees of craniocerebral trauma. Of particular interest were those patients clinically categorized as having sustained severe craniocerebral trauma, and in this group all those who had died received more critical evaluation. The patients with mild or moderate head injury, as well as those who survived with severe craniocerebral injury, served as control groups when an estimation of factors leading to death was made. In this regard there were two principal features: (1) disturbances in acid-base balance; and (2) alterations in respiratory cycle.

Twenty-nine patients were studied. There were 18 patients with severe craniocerebral trauma and 11 with mild or moderate head injuries. In each case, careful note was made of the type and character of respiration, and acid-base studies included daily determination of the blood pH, carbon dioxide content, plasma bicarbonate, blood urea, hematocrit, and various electrolytes in the blood. In the severe head injury group (18) 5 patients survived. In each of these surviving patients there was no alteration of the acid-base mechanism or the respiratory cycle. The remaining patients who had suffered severe craniocerebral injury all died, and all manifested varying degrees of change in the respiratory mechanism, as well as severe alteration in the acid-base balance. The primary prevailing disturbance was that of acidosis, respiratory or metabolic or mixed. In those patients with elements of metabolic acidosis, nitrogenous retention of a marked degree was evident. The change in pH at times was of a character that understandably was completely incompatible with life. In the group of mild and moderate head injuries without associated intracranial clots there were no deaths, and in no instances were there irreversible respiratory or metabolic changes.

It is apparent that in patients with severe craniocerebral injury associated with alterations of the respiratory mechanism and ventilatory capacity a severe metabolic disturbance, namely, uncompensated acidosis of all types, is a common factor. A single feature that distinguishes those cases which result in fatal issue from those in which survival is evident is that of the presence or absence of respiratory alterations and attendant uncompensated changes in the acid-base balance.

Discussion

DR. THOMAS I. HOEN: When Dr. Cook asked me to discuss this paper, I consented with some trepidation, for I feel that the explanation of these phenomena is in the province of the neurophysiologist. In lieu of an explanation, I shall simply make some comments. As you know, respiration is, in its simplest terms, a reflex mechanism, although it is a complicated reflex. It is stimulated in two main ways: one by an excess of CO_2 in the blood, which affects the respiratory center, and one by a deficiency of oxygen, acting through the carotid sinus mechanism. The reflex functions in this way under normal circumstances.

Under pathological conditions, the reflex can be interfered with in a number of ways. These ways are primarily in the order of three: The first is by anatomic destruction of the center, which we encounter in all types of head injury. Second, although an increase in the CO_2 of the

blood acts as a stimulus to respiration, an excessive increase in the CO_2 of the blood will paralyze the reflex center and act as a depressant. (This occurred in the case Dr. Cook referred to, with the airway obstruction.) Third, a change in the pH of the blood, whether due to the respiratory mechanism or to metabolic disturbances, may paralyze the reflex center. In other words, a great increase in acidemia of the blood is toxic to the reflex center in a way similar to the action of morphine and other drugs.

I am disappointed that body temperature was not mentioned, for we have found in similar cases that it directly affects the respiratory mechanism. An obvious reason is that increasing body temperature greatly increases oxygen demand; at a temperature of 105 F the oxygen consumption is increased 40% to 50%, so that even with an increased oxygen uptake there may still be an oxygen lack. Also, a distinction should be made between anoxia and ischemia of the respiratory center.

Personality Factors Influencing Rorschach Responses in Organic Brain Disease. Drs. Robert L. Kahn, Louis Linn, and Edwin A. Weinstein.

Efforts to establish Rorschach criteria diagnostic of brain disease have been unsuccessful to date. Marked variations are found when different criteria are applied to the same population or when the same criteria are applied to different populations. It is considered naive to assume that organic brain disease is an entity which will lead to a particular type of behavioral change. More consistent with the facts is the assumption that the behavior of a given patient is due to the interaction of a number of factors. In the present study the influence of the premorbid personality on Rorschach responses was investigated. The records of 22 patients with brain disease were studied. All showed such patterns of behavior characteristic of altered brain function as disorientation for time and place, reduplicative delusions, and paraphasic language changes. All had diffuse or bilateral electroencephalographic abnormalities. The patients were divided into two groups according to the presence or absence of explicit verbal denial of illness (anosognosia). Since previous studies had demonstrated a relationship between explicit denial and a particular type of premorbid personality, this division of the patients provided a means of studying the effect of different personality patterns. The results showed marked differences between the two groups. The patients with explicit verbal denial gave significantly fewer movement, shading, color, and small detail responses and a lower total number of responses, while giving a significantly larger percentage of form and animal responses. These differences correspond to differences in the pattern of premorbid personality found on interviews with members of the family. The results of this study are considered a further indication that the Rorschach test can have only limited usefulness as a diagnostic tool for brain disease when applied mechanically according to an arbitrary set of criteria or signs.

Discussion

Dr. Fred Brown: In this paper, we are treated to challenging hypotheses concerning the usefulness of the Rorschach test as a diagnostic tool in detection of brain disease, and have been shown that premorbid personality structure is a crucial differentiating factor in determining the Rorschach patterning and in accounting for the wide range of configurations encountered in this area, a range which has caused some psychodiagnosticians to throw up their hands in complete and frustrated surrender.

Quite apart from the basic hypothesis and its far-reaching implications, it is important to note that the authors make no conclusive comment with regard to the use of the Rorschach test as a diagnostic device for detection of brain pathology. They state that it has limited usefulness as a diagnostic tool for brain disease when applied mechanically according to an arbitrary set of criteria or signs. Does this mean that there is a less mechanical and more dynamic way of using the Rorschach test for this purpose? Certainly there is no intention of offering the patterns presented on the slides as a guide.

Dr. Louis Linn: Many years ago it became apparent that the Rorschach test by itself was not a reliable test of organic brain disease. At times the test was helpful; at other times it was not. There seemed to be no way of understanding its variability until the work of Weinstein and Kahn suggested the idea of separating our records into two groups—those of patients with anosognosia (explicit verbal denial of illness) and those of patients without anosognosia. As soon as we did that, it immediately became clear that the anosognosic group showed Piotrowski's signs of organic brain disease and the nonanosognosic group did not. In retrospect, it seems extraordinary that a consideration of premorbid personality factors

should have been omitted from the analysis of Rorschach records of patients with organic brain disease, since the Rorschach test is, above all, one of personality.

Dr. Brown questioned the extent to which our records reflected basic personality and the extent to which it reflected the organic disturbance per se. In a few cases we were able to repeat the Rorschach test after the pathologic brain process had improved and the disturbance of consciousness was no longer present. In these instances there was relatively little change in the pattern of the Rorschach responses, so that we felt even more justified in concluding that the Rorschach differences we saw reflected most of all differences in basic personality.

It should be emphasized that psychological studies are important in the diagnosis of organic brain disease. However, it is ill-advised to rely exclusively, or too heavily, on the Rorschach test by itself.

The Abuse of the Psychological in Clinical Psychiatry. Dr. Gregory Zilboorg.

The fact that ours is a psychological age is incontestable. Yet there are signs that a considerable change is taking place in the character of this psychological age. During approximately the last decade and a half we seem to have shifted away from "pure psychology" and to have drifted imperceptibly, but relentlessly, into a form of pharmaceutic interference with clinical conditions.

Important and instructive as the historical parallel of the use of tranquilizing drugs some 140 years ago may be, we are not as devoid of psychological insight into the problems of our patients as, for instance, Heinroth and Reil were, when they relied so much on the tranquilizing drugs of their day.

I am not an opponent of the use of certain modern drugs, but I am opposed to coupling their use with the idea that they are adjuvants to psychotherapy. It is from this point of view that I consider that psychology is abused if it is made to fit our psychotherapeutic wishes in the light of our medicamentous propensities. As the awareness of this becomes greater and clearer, the main trends of medical history cannot help reasserting themselves and reinstating the value and the autonomy of the human individual. Throughout the ages medicine has never failed in such moral revival. It was thus in the 13th and 16th centuries, and will thus be in this or the century ahead of us.

Discussion

Dr. Oskar Dietheim: It is with some hesitancy that I shall try to add a few points to the very inconclusive, provocative, and highly constructive presentation by Dr. Zilboorg. Zilboorg as the historian shows a certain pessimism that seems to me unjustified when we consider the sound progress that has been made in the last 50 years. Zilboorg as a clinician gives encouragement and optimism in his discussion in which he presents the essence of psychotherapy. Remarkable progress has been made in psychological understanding and in the emphasis on the individual personality. We recognize now the need to study psychological development, the relationship to the environment, the interpersonal factors, and cultural aspects.

Dr. Louis Linn: Dr. Zilboorg raised the question whether it is possible to conduct psychotherapy in a case in which the ego function has been modified by organic means. In my opinion, the answer is "yes." First, we must ask, "What is psychotherapy?" I consider psychotherapy in its broadest sense, and include the beneficial influences which are derived from school, from work, from contact with loving friends and relatives, and from recreation and other constructive influences in the community, as well as the changes which the psychiatrist himself can effect via direct psychotherapeutic influences.

Dr. Zilboorg raised the question whether psychotherapy can ever be conducted on a patient in whom the full ego is not participating. I would say that all psychotherapy takes place in such a setting. This is the essence of mental illness: that the ego, such as it exists, is not a full ego, but a constricted, defensive structure, in which full potentialities are not being realized. What results from psychotherapy is a process of ego growth.

I have seen depressed patients go into remission after three or four shock treatments, and remain in remission for years thereafter, long after all organic effects of the shock therapy have worn off. What impresses me is that these patients emerge from their illness with the same defenses they would have employed had the psychosis been permitted to run its course without shock therapy. The task for the psychotherapist is essentially the same whether or not shock therapy has been used to shorten the psychosis. For these reasons, I do not believe that

the proper use of organic methods in psychiatric treatment constitutes a regressive development.

DR. PHILIP R. LEHRMAN: I wish to express my appreciation of the opportunity of hearing the brilliant paper of Dr. Zilboorg. There is only one thought I wish to express in reference to the various pharmaceutic and surgical treatments of psychological disorders. These therapies divert the patient's, as well as the physician's, "return of the repressed," and in this way aid in strengthening the repressions. This is not a new idea and I'm sure Dr. Zilboorg is fully aware of it.

DR. ALVIN RALPH MILLER: Would Dr. Zilboorg recommend Freudian psychoanalysis for anyone with overwhelming emotional conflicts? Does he feel psychoanalysis is the only answer?

DR. GREGORY ZILBOORG: Dr. Diethelm is temperamentally optimistic, and I am pessimistic, but there are no essential differences in our points of view.

Dr. Linn has raised a question which it would be a shame to leave unanswered or undiscussed. I did not say "the participation of the full ego." No ego is ever complete, particularly in disease. I said "with full participation of the ego forces available," and I think that when you use a drug as an adjuvant you reduce the availability of those forces.

One word is left, and this is an objection. I regret that people use the term "interpersonal relations." I do not know of any relation of any person to anything that is anything but interpersonal. I do not believe there are "interpersonal" relationships which are distinguished from other relationships of the individual. I think all psychiatric thought should be centered on the human being as an individual, a concept which includes everything in him in relation to himself as well as in relation to the outside world.

NEW YORK NEUROLOGICAL SOCIETY, AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

GEORGE H. HYSLOP, M.D. President, New York Neurological Society, Presiding

Joint Meeting, March 13, 1956

A Familial Form of Neuropathy (Charcot-Marie-Tooth) with Gastrointestinal Symptomatology. DR. MURRAY E. MARGULIES and DR. IRIS F. NORSTRAND.

A family of Greek extraction was studied in which three generations were afflicted with a degenerative disease of the nervous system akin to the Charcot-Marie-Tooth type of peroneal muscular atrophy. The maternal grandfather of this family is reported to have died in the third decade of life, with a widespread muscular atrophy and diarrhea of many years' duration. His daughter, who also had muscular atrophy, with weakness and numbness of the legs, and diarrhea, died at the age of 37. Her husband died at the age of 69, of pneumonia. Five of their seven offspring developed in early adult life muscular atrophy, with weakness of the extremities and sensory symptoms. Four of the children had recurrent distressing attacks of diarrhea. The fifth sibling did not have diarrhea, but from early boyhood was subject to nausea and vomiting.

The neurologic picture in all cases seemingly affected the spinal cord, nerve roots, and peripheral nerves. In two of them the diagnosis of the Charcot-Marie-Tooth type of neuritic muscular atrophy was entertained. In another instance the diagnosis of hypertrophic interstitial neuritis of Dejerine and Sottas was made but was not confirmed by biopsy. Laminectomy in the fourth case revealed central gliosis in the cervical segments, though there was undoubted evidence of peripheral nerve involvement in this case clinically. Postmortem examination in the fifth case disclosed degenerative changes in the ventral horn cells of the spinal cord, but limited autopsy studies revealed nerve root disease as the only corroboration of the peripheral nerve symptomatology present during life. No basis for the gastrointestinal symptoms could be ascertained. It seems justified to postulate that in this family, with a widespread disorder of lower motor neuron, sensory, and spinal cord function, there is also present a similar disturbance involving the autonomic nervous system.

Dystonic Amyotrophy. DR. ISRAEL S. FREIMAN and DR. JOACHIM LUWISCH.

This report concerns two patients, both men, who presented an unusual clinical syndrome characterized by dystonia, generalized muscular atrophy of severe degree, pyramidal tract signs, and no mental changes. The first patient is 49 years of age. His trouble began at the age of 30 with involuntary movements, which gradually and slowly increased through the years. Later generalized atrophy and weakness developed. He had pes cavus. His lower limbs were markedly thin up to the lower third of the thighs, giving the appearance of stork legs. Deep reflexes were

abolished except for a 1+ right knee jerk. Nevertheless, he has a bilateral Babinski sign. He is able to get on his feet and to walk with difficulty, but is wheel-chair-ridden because of severe dystonia, which develops when he is on his feet. There is severe weakness in the arms. No sensory changes were elicited. Recently, within the past few months, the greater auricular nerves in the neck have been found palpable, and a few small nerves on the dorsum of one hand are thickened and firm. Biopsy of muscle indicated mild changes characteristic of neural muscular atrophy.

The second patient is 48 years of age, and his trouble began at the age of 26, also with involuntary movements, which gradually and slowly progressed and are now present and severe when on his feet. Later he developed generalized muscular atrophy, which is now widespread. This patient has widespread hypertrophy of peripheral nerves, which are both visible and palpable in the neck, in the hands, and in the feet. He has bilateral pyramidal tract signs. His deep reflexes are overactive. There is loss of vibratory sense in all four limbs, to the iliac crests and to the elbows, and along the vertebral column to the 12th thoracic vertebra. Position sense is greatly impaired in both lower limbs. Sensation is intact to pinprick. Laboratory findings, including serology, have been essentially normal. Biopsy of peripheral nerves and muscle disclosed neuritic muscular atrophy of moderate degree and mild degeneration of peripheral nerves, with considerable hyperplasia of Schwann cells.

In the family histories of these patients there is some evidence pointing to a genetic disorder. The first patient is the product of a consanguineous marriage, and a few members of both families have congenital disorders of various kinds. We believe that these two patients represent sporadic cases of a heredodegenerative disorder involving the extrapyramidal motor system, pyramidal systems, and peripheral nerves.

This paper appeared in full in the February, 1956, issue of *Neurology*.

Discussion

DR. ABRAHAM M. RABINER: One could dismiss these two papers as very interesting in that the first concerned a family group with the Charcot-Marie-Tooth type of neuritic muscular atrophy which also had gastrointestinal symptoms, and the second reported patients who had dystonia musculorum deformans and also generalized muscular atrophy.

Both presentations direct attention to an extremely important facet of the mechanisms underlying the development of many of these so-called heredodegenerative diseases. There is an inherent defect in the vitality of the structures affected. An exogenous agent may at times be an etiologic factor by adversely affecting such structures. Gowers spoke of this as premature decay. Exogenous agents are not selective in their attack on neural structures. In these groups there is usually involvement of the motor systems, as well as impairment of proprioception. We know that these structures all participate as a team in the function of locomotion and the maintenance of erect posture. The clinical picture results from attack and disintegration of this function, and is not an exogenous attack on random structures.

DR. S. BERNARD WORTIS: I agree with Dr. Rabiner regarding our need to study and know more about the factors concerned in these so-called heredodegenerative diseases. I am not so sure that these syndromes all represent premature aging, causing tissue breakdown, because modern genetics is concerned with genes and the effects of environmental stresses on genes during crucial metabolic periods.

The patients' illnesses fall into a group in which the etiology is not known, and I hope we are not going to add any more physician-named syndromes to our already overcrowded list of obscure syndromes.

In the muscular atrophies there are three groups: those with absence of involvement of the central nervous system, in which the muscles alone are the seat of the disorder. We do not know the metabolic cause of these atrophies. The second group is one in which the etiology is equally obscure, in which muscle wasting is secondary to destruction of the motor neurons, with nuclear degeneration, and the third group consists of the chronic productive wasting diseases, due to involvement of the peripheral nerves; the cases described here showed this very clearly.

In this entire group we are dealing with etiologies that need genetic and metabolic elucidation. There are related heredodegenerative diseases, including torticollis, status dysmyelinatus, double athetosis, spastic pseudosclerosis, and pigmentary degeneration of the globus pallidus, in which our knowledge of what causes death and disease of the tissue of the nervous system and/or the muscular tissue is as yet entirely obscure. Although in the muscular dystrophies, to use an example, we describe and label several subgroups according to age of onset, presence or absence

of pseudohypertrophy, distribution of muscular atrophy, etc., there is really no justification for these various subdivisions, since many or all are merely variations in the clinical picture of a single disease process.

Advances in our knowledge of these illnesses await more exact biochemical knowledge in the field of genetics.

Follow-Up Studies on Circular Manic-Depressive Reactions Occurring in the Young. DR. ALLISON B. LANDOLT.

Sixty patients between the ages of 15 and 22 with a disease initially diagnosed as manic-depressive psychosis, circular type, at the New York Hospital-Westchester Division were followed in an attempt to determine the outcome of their difficulties.

Seventy-five percent of them had positive family histories of mental instability in antecedents or collaterals, and one-third of those studied showed schizoid coloring prior to or during their initial illness. None of these factors appeared significantly to affect the eventual prognosis in a statistically valid manner.

Nine of these patients later developed overt schizophrenia, all of the catatonic type.

Twenty-seven patients have continued to exhibit typically affective symptomatology, and two more have continued to have mood swings for a few years but have had no problems in a decade.

No information could be obtained from 5 people included in the study, and statistically inconclusive data were received on 11. Emotional instability was indicated, but no diagnostic inferences could be drawn.

A most interesting statistic appears to be the apparent absence of suicide in the usually accepted sense among the group studied.

Ten patients must now be considered as completely recovered, and six of these have had no recurrence following their initial hospitalization.

Discussion

DR. ROBERT B. MCGRAW: We are indebted to Dr. Landolt for again bringing this very old problem to our attention. It is very much with us. I was astonished about a year ago to have a psychiatrist tell me that he did not believe there was such a clinical entity as manic-depressive psychosis and had never seen a case. I have seen a great many, and they do present all the variations which Dr. Landolt has brought to our attention. He brings again to our minds the question whether we should consider these cases as mostly manic-depressive, and partly schizophrenic, or mostly schizophrenic and partly manic-depressive, and therefore whether we do have such combinations of these two types of illness. Of further importance is the absence of suicide in this rather large group. To focus on the future, I would hope that studies will be made in which cases of manic-depressive psychosis without admixture of the schizophrenic type of reaction would be more carefully studied, both from the clinical and from the biological and physiological standpoints. I should like to suggest that such studies be made.

DR. S. BERNARD WORTIS: Since Dr. Landolt's group was studied between 1930 and 1949, and partly antedated the intensive use of convulsive electroshock and insulin therapy in this country, I should like to ask whether there was any difference in the recovery rate and the type of recovery with different therapeutic methods.

I can support his statement that we are seeing much less manic-depressive psychosis in psychiatric hospitals. I do not know why, but our rates at Bellevue have been cut down about 40%. This may be due to the newer therapeutic methods, so that the patients are not brought to the hospital. There may, however, be other factors, one being the recent tendency to use the diagnosis of schizophrenia more frequently than it was years ago. Would Dr. Landolt comment on these points?

DR. GEORGE H. HYSLOP: In regard to the disappearance nowadays of manic-depressive psychosis, I think much of this is a matter of semantics and that certain schools of clinical psychiatry will seize upon a fractional part of a clinical picture and give a title to it which perhaps does not belong.

DR. ALLISON B. LANDOLT: In answer to Dr. Wortis' question: Most of these patients actually were in the hospital in the 1930's, when we did not use electroconvulsive or insulin therapy. I had a great deal of difficulty finding manic-depressive psychoses from 1945 on. Most of these patients have been followed up for from 15 to 25 years. For the few who had electroshock therapy there did not seem to be any specific statistical validity as to the final outcome. They continued to have mood swings. The therapy did not appear to alter the essential course.

I cannot say why there are fewer cases of manic-depressive psychosis, except that, as Dr. Hyslop suggests, it is a question of semantics. Today frequently the slightest sign of schizophrenic coloring will be diagnosed as schizophrenia, regardless of whether the patient has a mood swing or not, and that may account for more diagnoses of schizophrenia than of manic-depressive psychoses. We seem to be more interested in schizophrenia.

DR. JOACHIM LUWISCH: I wonder whether the answer may be found in the fact that these manic-depressive psychoses are seen first as depressions; then the patients are given shock treatment, and they do not enter the manic phase.

DR. GEORGE H. HYSLOP: Dr. McGraw, you see a large number of patients treated with shock; do you think there are fewer manic-depressives now?

DR. ROBERT M. MCGRAW: As to whether there is fewer or more cases of manic-depressive psychosis now than there were, I should hesitate to say. As to whether the treatment prevents, or stops, a further attack in any great percentage of cases I shall have to say I do not think it does, though we know of many cases in which we have treated the patients a long time ago with electroshock and they have had no more attacks; but we also have seen cases, as Dr. Landolt has shown, in which no electroshock treatment was given and the one attack has been the only attack.

DR. GEORGE H. HYSLOP: Dr. McGraw, Dr. Luwisch's question was whether shock treatment for a depression prevented a manic phase swing of so-called circular type.

DR. ROBERT B. MCGRAW: I think there may be some truth in it, and that is about as far as I can go in answering that question.

Illness, Attitudes, and Behavior Patterns in a Group of "Healthy" Chinese. DRS. FRANCIS D. KANE, PETER RICHTER, LAWRENCE E. HINKLE JR., and HAROLD G. WOLFF.

This study is one of a series to determine which features of man's relationship to his environment are pertinent to his health.

One hundred Chinese were studied as representing a relatively homogeneous group of ostensibly healthy people who had undergone dislocation from their culture, social life, close interpersonal relationships, and geographical location. They were mostly students and professional people who had been in this country 5 to 10 years. The study was made by anthropologists, sociologists, psychologists, internists, and psychiatrists.

The findings were that 25% of the group had 53% of illness episodes. Illness episodes cluster. Clusters are typified by involvement of all body systems and all etiologies and major and minor illnesses. Clustering is not predictable on the basis of change per se; clustering is predictable on the basis of the informant's own statements of the life situation being stressful. These findings are comparable to American groups.

Psychopathology is comparable to that found in American culture. There is a correlation between (1) a person's sense of continuity about his life and his health and (2) statements of discontinuity and illness. These statements were made independently of descriptions of illness episodes or dislocations.

Abstracts from Current Literature

EDITED BY BERNARD J. ALPERS

Physiology and Biochemistry

ROLE OF PHOSPHORYLCHOLINE IN ACETYLCHOLINE SYNTHESIS. J. F. BERRY and E. STOTZ, J. Biol. Chem. 218:871, 1956.

It has been suggested that phosphorylcholine appeared during acetylcholine synthesis by extracts of acetone extracts of brain. An enzyme cholinephosphokinase has been isolated from brain which catalyzes the formation of phosphorylcholine and adenosinediphosphate from choline and adenosinetriphosphate. Berry and Stotz find that phosphorylcholine is more active than choline as a precursor for acetylcholine synthesis in rat brain extracts. Omission of ATP nearly abolished acetylcholine synthesis when choline was employed as substrate, but caused only slight depression of synthesis when phosphorylcholine was employed. Omission of coenzyme A, however, elicited clear reduction of acetylcholine formation when phosphorylcholine was employed.

PAGE, Cleveland.

THE OPTIC NERVE SHEATH PATHWAY. SEYMOUR LEVINE and MELVIN BRONSTEIN, A. M. A. Arch. Ophth. 54:369 (Sept.) 1955.

Levine and Bronstein state that there is a continuity of the cranial, subdural, and subarachnoid spaces with the corresponding spaces around the optic nerve. Colloidal material and nondivisible dyes injected into the cranial subarachnoid space reached the optic nerve sheath. Intracranial cerebrospinal fluid pressure is transmitted to the space around the optic nerve. Transmission of particulate matter through the optic nerve sheath is suggested by the presence of inflammatory cells in cases of meningitis.

SPAETH, Philadelphia.

CERVICAL SYMPATHETIC GANGLIONECTOMY AND AQUEOUS FLOW. ERIK LINNER and EMILE PRIJOT, A. M. A. Arch. Ophth. 54:831 (Dec.) 1955.

The role of the sympathetic nervous system in the regulation of intraocular pressure has been studied by many investigators, with varied and contradictory results. The authors studied the effect on intraocular pressure of extirpation of the superior sympathetic ganglion in rabbits. On the first day after operation the intraocular pressure on the side of the operation was reduced to the level of the episcleral venous pressure. This decrease in aqueous outflow pressure suggested a marked decrease in rate of aqueous flow, indicating that an adrenergic mechanism may be involved in the intraocular secretory process. All the changes disappeared a few days later, with complete restoration of normal tension and normal intraocular fluid physiology.

SPAETH, Philadelphia.

EDROPHONIUM (TENSILON) IN DIAGNOSIS OF OCULAR MYASTHENIA GRAVIS, S. ARTHUR BORUCHOFF and BERNARD GOLDBERG, A. M. A. Arch. Ophth. 53:718 (May) 1955.

Myasthenia gravis frequently involves the extraocular muscles. Indeed, disturbances in these structures may be the earliest, or even the only, signs of this disease. Boruchoff and Goldberg call attention to a new drug which they consider a rapid, safe diagnostic test for the investigation of cases of suspected myasthenia gravis. The positive response when it appears is dramatic, and a myasthenic who gives a negative response on testing with neostigmine may respond dramatically to edrophonium. The drug edrophonium chloride (Tensilon) is a quaternary ammonium compound. Although it has some action as an anticholinesterase compound, its primary mode of action is direct stimulation of the myoneural junction.

SPAETH, Philadelphia.

N-ACETYL-L-ASPARTIC ACID IN BRAIN. H. H. TALLAN, S. MOORE, and W. H. STEIN, J. Biol. Chem. 219:257, 1956.

Relatively large amounts of bound aspartic acid have been found in cat's brain, which represented the largest quantity of conjugated amino acid of unknown nature found in any of the protein-free tissue extracts studied. The conjugate has now been identified as N-acetyl-L-

aspartic acid. It occurs in concentrations of the order of 100 mg. per 100 gm. in both cat's and rat's brain and is not present in appreciable quantities in cat's liver, kidney, muscle, or urine.

PAGE, Cleveland.

ON THE MECHANISM OF DEHYDROGENATION OF FATTY ACYL DERIVATIVES OF COENZYME A: 1. THE GENERAL FATTY ACYL COENZYME A DEHYDROGENASE. F. L. CRANE, S. MII, J. G. HAUGE, D. E. GREEN, and H. BEINERT, J. Biol. Chem. 218:701, 1956.

Fatty acid acyl CoA derivatives are first dehydrogenated to the corresponding α, β unsaturated compound. Two separate enzymes can catalyze this dehydrogenation. One of these has already been characterized as a cuproflavoprotein by Mahlor. The second one is the concern of this paper. It is a flavoprotein and acts on acyl CoA derivatives from C_4 to C_{18}. The enzyme is obtained from pig-liver mitochondria. A similar enzyme has been prepared from beef liver. Still a third yellow flavoprotein has been discovered which is specific for fatty acyl CoA derivatives of long carbon chain. It has been called palmityl CoA dehydrogenase.

PAGE, Cleveland.

Neuropathology

A CLINICO-PATHOLOGIC REPORT OF AN ACUTE FAMILIAL ENCEPHALOPATHY IN THE NEWBORN INFANT. CHARLES F. BARLOW, J. Neuropath. & Exper. Neurol. 14:413 (Oct.) 1955.

Barlow reports on two infant siblings with similar clinical courses and essentially identical histopathologic findings. Both died in the second day of life, during the latter part of which they had convulsions, facial twitchings, and episodes of cyanosis. The neurons everywhere showed extensive alterations. In the cortex, fatty vacuoles, displacement of the nucleoli, and fragmented nucleolar chromatin were seen. Neurons of the basal nuclei were swollen. Astrocytes were numerous and vesicular and showed clasmatodendrosis. Although the mother had had toxoplasmic chorioretinitis, no evidence of this disease was encountered in the infants. While Barlow believes these unusual findings are probably nonspecific, he suggests a metabolic defect.

SIEKERT, Rochester, Minn.

OSSIFICATION IN GLIOMAS. J. BEVIN and J. S. TYTUS, J. Neurosurg. 12:577 (Nov.) 1955.

Bebin and Tytus report the occurrence of bone formation in two cases of intracranial glioma. In the first case, histological examination revealed the presence of well-differentiated bone formation in an astrocytoma of the cerebellum, and in the second case bone was found in an oligodendroglioma of the right frontal lobe.

The presence of bone formation within intracranial neoplasms, particularly within gliomas, arouses speculation as to the origin of osseous tissue. In meningiomas, it has been suggested that bone formation occurs secondary to degeneration of tumor cells or that bone is formed by the multipotential cells that make up the tumor itself. Since gliomas are derived from neuroectodermal tissue, this explanation is not feasible, for it is difficult to accept the origin of osteoblasts from necrotic cells themselves. The authors postulate that in pathological conditions, metaplastic bone formation might occur within the areas of calcified normal or necrotic tissue by direct transformation of mesenchymal cells of the blood vessels into osteoblasts, or they might arise from fibroblasts and reticular cells.

MANDEL, Philadelphia.

Meninges and Blood Vessels

THE PROBLEM OF SPONTANEOUS SUBARACHNOID HEMORRHAGE WITH PROVEN ANEURYSMS. DWIGHT PARKINSON, J. Neurosurg. 12:565 (Nov.) 1955.

Parkinson reports 60 consecutive cases of spontaneous subarachnoid hemorrhage in normotensive persons who survived their initial episode. In this group, 38 aneurysms were demonstrated by angiography, 33 being saccular and 5 arteriovenous. Eight patients with saccular aneurysms refused surgery, and seven of these persons died within one to five years as a result of recurrent hemorrhage from the aneurysm. The remaining 30 aneurysms were operated upon by direct intracranial approach, and in this group four died postoperatively and one patient became hemiplegic. In three of the four deaths, the patients were operated upon while in coma, and multiple aneurysms were demonstrable in two of these cases. The fourth patient died, apparently of inadequate anterior cerebral circulation. No recurrent hemorrhage occurred in the surgically treated cases.

Five patients had arteriovenous aneurysms, and they were all treated by complete surgical excision. There were no deaths in this group.

In 22 of the 60 cases, no aneurysm was visualized with bilateral carotid angiography, and there was no recurrent hemorrhage in any of these cases. Two patients died of other causes, and no aneurysm was demonstrable. Failure to visualize an aneurysm by angiography does not exclude an aneurysm at autopsy.

Parkinson concludes that surgery is the treatment of choice in cases of spontaneous subarachnoid hemorrhage with a proved aneurysm, for death is a frequent complication of conservative management with demonstrable aneurysms.

MANDEL, Philadelphia.

Diseases of the Brain

HYSTERICAL AMBLYOPIA. T. F. SCHLAEGEL JR. and F. V. QUILALA, A. M. A. Arch. Ophth. 54:875 (Dec.) 1955.

Schlaegel and Quilala report a statistical analysis of 42 cases of probable hysterical amblyopia, using as their criterion for this diagnosis the finding of tubular fields.

They found 42 instances of tubular fields; of these, 10 were found in institutional cases and 32 in noninstitutional cases. Sex played no significant role from a statistical standpoint. Corneal sensitivity was significantly lower among the patients with tubular fields. The degree of contraction of the tubular fields was analyzed. In the majority of cases, over 52%, the fields were severely contracted. The age of the patients relative to this finding was not of statistical significance. In only one patient was a unilateral field tubular. Thirty-three cases were bilateral. Five of the patients had only one eye, and three patients had a combination of tubular and spiral fields. The authors state that "reduced visual acuity was the commonest presenting complaint, but some had no eye complaint." They state, further, that "although amblyopia is commonly associated with tubular fields, the visual acuity as a result of refraction was 20/20 or better in 48% of our cases. The vision is frequently easily improved by such suggestion and encouragement."

SPAETH, Philadelphia.

CORTISONE AS AN AID IN THE SURGICAL TREATMENT OF CRANIOPHARYNGIOMAS. JOHN S. TYTERS, HOLBROOKE S. SELTZER, and EDGAR A. KAHN, J. Neurosurg. 12:555 (Nov.) 1955.

The surgical treatment of craniopharyngiomas has been accompanied by a high mortality rate in the past, particularly when total removal of the tumor was attempted. The close relationship between the craniopharyngioma and the hypothalamus frequently exposes the latter to trauma, which may contribute to the high mortality, as well as the long-standing pressure effect of the tumor upon the pituitary gland itself.

The authors report a series of 21 cases of craniopharyngiomas in which the tumor was removed as completely as possible. Six patients were not given cortisone and died within 48 hours of their craniotomy either from hyperthermia or from peripheral vascular collapse, and a seventh patient had persistent hyperpyrexia and died on the 10th postoperative day. Seven others who did not receive cortisone preoperatively survived, thereby making a 50% mortality rate among the patients who did not have cortisone. All seven of the patients who received cortisone during the preoperative period survived the initial postoperative period. The authors believe that cortisone administered before and after surgery reduces the operative mortality by preventing postoperative adrenocortical collapse and preventing postoperative hyperthermic crises by minimizing postoperative edema.

MANDEL, Philadelphia.

REPORT ON 280 CASES OF VERIFIED PARASAGITTAL MENINGIOMA. G. F. HOESSLY and H. OLIVECRONA, J. Neurosurg. 12:614 (Nov.) 1955.

Hoessly and Olivecrona report 280 parasagittal meningiomas which occurred among 1004 verified meningiomas. Of the 280 patients, 276 underwent surgery, and 34 (12.3%) failed to survive the operation. Complete obliteration of the superior longitudinal sinus was found in 48 cases, and partial obliteration was noted in 96 cases; with a conservative attitude toward bloc resection of the partially patent sinus the mortality rate decreased. The principal cause of postoperative death was cerebral edema, whereas prior to 1947 most of the postoperative deaths were due to blood loss, as a result of inadequate replacement methods. After five years, a majority of the patients were still living, and 24% died. In this series, 17 patients were operated

upon for a second time, and 4 patients returned for a third operation because of recurrence of the tumor.

Arteriography was found to be of greater value than air studies in the diagnosis of meningioma. Separate injections of the internal and external carotid arteries are recommended to determine the vascularity of the tumor.

MANDEL, Philadelphia.

THE OCULAR SIGNIFICANCE OF INTRACRANIAL CALCIUM DEPOSITS. JOSEPH E. ALFANO and HARVEY WHITE, A. M. A. Arch. Ophth. 54:77 (July) 1955.

Pathological intracranial calcifications are seen in toxoplasmosis; Sturge-Weber syndrome; tuberous sclerosis; intracranial aneurysms; slow-growing tumors, such as gliomas and meningiomas, craniopharyngioma, and pituitary adenoma; hypoparathyroidism; arteriovenous malformations; subdural hematoma, and parasitic conditions. In addition, miscellaneous conditions in which calcifications are sometimes found include encephalitis, lead intoxication, extreme old age, amaurotic idiocy, epilepsy, chordomas, cholesteatomas, ependymoma, and old intracranial abscesses, tuberculomas, and hematomas.

Alfano and White report 10 cases with intracranial calcifications, including a meningioma of the left parietal region and cases of toxoplasmosis, macular chorioretinitis, tuberous sclerosis, Parkes-Weber-Dimitri syndrome, fibrillary astrocytoma, mental retardation without physical findings, craniopharyngioma, and saccular aneurysm.

SPAETH, Philadelphia.

SOME INSTRUCTIVE MANIFESTATIONS OF CHIASMAL DISEASE. JOHN P. WENDLAND, A. M. A. Arch. Ophth. 54:13 (July) 1955.

When one considers that approximately 25% of brain tumors either lie in or about or involve the optic chiasm, the relationship which impairment in vision plays to the diagnosis of such lesions becomes clear. Wendland emphasizes the importance of certain manifestations of chiasmal disease in three well-known lesions of the chiasm: pituitary adenoma, chiasmal arachnoiditis, and chiasmal glioma. He stresses the significance of field changes. These are (1) the absolute diagnostic significance of bitemporal hemianopsia, central or peripheral, as the result of midline or infrachiasmal disease; (2) central or centrocecal scotoma combined with a temporal field defect in the opposite eye, due to a lesion of the chiasm at the junction of the optic nerve and the chiasm, the lesion being ipsilateral to the scotoma; (3) blindness in one eye with temporal hemianopsia in the other, the lesion being on the side of the eye which is blind; (4) grossly incongruous homonymous hemianopsia from a lesion on the side of the chiasm at its junction with the optic nerve anteriorly or the tract posteriorly.

SPAETH, Philadelphia.

HYDROCEPHALUS ASSOCIATED WITH CHOROID PLEXUS PAPILLOMAS. JOSEPH F. SMITH, J. Neuropath. & Exper. Neurol. 14:442 (Oct.) 1955.

Smith reports two cases of choroid-plexus papilloma of one lateral ventricle associated with hydrocephalus. In one case basal meningitis with resultant obstruction could be excluded. In the other examination could not exclude chronic meningitis, although it seemed unlikely. It is believed that the hydrocephalus was the result of oversecretion of cerebrospinal fluid by the tumor.

SIEKERT, Rochester, Minn.

NEUROFIBROMATOSIS AND CONGENITAL UNILATERAL PULSATING AND NONPULSATING EXOPHTHALMOS. ANDRE J. BRUWER and ROBERT R. KIERLAND, A. M. A. Arch. Ophth. 53:2 (Jan.) 1955.

Twelve years ago a survey was made of 812 cases of pulsating exophthalmos (Martin, J. D., Jr., and Mabon, R. F.: Pulsating Exophthalmos: Review of All Reported Cases, *J. A. M. A.* 121:330-335 [Jan. 30] 1943). In practically all these cases an arteriovenous shunt was apparently the basic factor responsible for the condition. At that time no mention was made of a smaller group of cases of congenital unilateral pulsating exophthalmos in which there is no associated arteriovenous shunt but in which the roentgenologic findings are indicative of pathology of the sphenoidal and orbital portions of the frontal bone. In these instances the pathology is due to neurofibromatosis.

SPAETH, Philadelphia.

Diseases of the Spinal Cord

HEMANGIOMA OF A DORSAL VERTEBRA WITH COLLAPSE AND COMPRESSION MYELOPATHY. ROBERT BELL, J. Neurosurg. 12:570 (Nov.) 1955.

Hemangioma of the vertebral column is encountered occasionally as an incidental finding. Although many such hemangiomas are regarded as being innocuous clinically, a few undergo proliferative and degenerative changes. By x-rays, a hemangioma is characterized by columniation of the centrum of a vertebra. It has been proposed that expansion of the tumor results from endothelial budding and subsequent canalization of the outgrowths. Cancellous bone encroached upon by these newly formed channels assumes the irregular colonnade effect that is readily identified by roentgen examination. The trabeculae frequently become enlarged to three times normal size.

Bell reports a case of a 25-year-old white woman who complained of radicular pain in the back and weakness of both legs. Neurological examination revealed a spastic paraplegia of the legs with a bilateral Babinski sign and a sensory level at T-11-dermatome zone. Roentgenograms of the thoracic spine showed moderate decalcification of the body of the 10th thoracic vertebra with reactive tubercula in parallel. A laminectomy was performed, and the vertebral canal was found to be encroached upon by the thickened lamina. Microscopic examination revealed the tumor to be a cavernous hemangioma of bone. The patient subsequently showed signs of cord compression, and a second laminectomy was performed two years later, following which she gradually recovered the complete use of the legs.

Bell states that the sequence of clinical events in this case serves to caution one against overestimating the strength of a vertebra involved by angioma. Partial collapse of a vertebral body involved by an angioma is an indication for fusion. Roentgen therapy may be of help postoperatively, but it should not be considered the recommended treatment for hemangiomas in the presence of an advancing paraparesis.

MANDEL, Philadelphia.

PROGRESSIVE FAMILIAL ATAXIA. M. A. NEUMANN and R. COHN, J. Neuropath. & Exper. Neurol. 14:398 (Oct.) 1955.

Neumann and Cohn report their findings in the central nervous system in a patient with ataxia, spasticity, and weakness: demyelination of the olivopontocerebellar pathways, both spinocerebellar and both spinothalamic tracts, and the upper portion of the funiculus gracilis; degeneration of the ventral horn cells and Clarke's column, and fibrosis of the ventral and dorsal spinal nerve roots. On the basis of this case and the literature, they suggest that many cases are "transitional" and that an effective classification would be cerebellar system disease with qualifying designations, depending on the elements involved.

SIEKERT, Rochester, Minn.

DIAGNOSIS AND TREATMENT OF MYELOPATHY DUE TO CERVICAL SPONDYLOSIS. D. W. C. NORTHFIELD, Brit. M. J. 2:1474 (Dec. 17) 1955.

Northfield reviewed the results of surgical treatment of 39 patients with spondylotic myelopathy, ranging in age from 30 to 70 years. In all patients the disease had produced compression of the cord by intraspinal osteophytes and ischemia by interference with its blood supply. The duration of symptoms before treatment ranged from 6 weeks to 20 years. The commonest initial symptom, weakness or stiffness of one or both legs, occurred in 15 patients. Twenty-seven patients had severe spastic weakness of the lower extremities. All but two patients noted weakness, wasting, flaccidity or spasticity, and increase or decrease of tendon reflexes in the upper extremities. Sensory disturbances were detected in most of the patients. Only a few complained of difficulty with micturition, but this was never severe. The diagnosis was made by radiography, including myelography. The patients were treated by laminectomy. The arches above and below the disc were removed; the ligamenta denticulata were divided, and, when necessary, the intervertebral foramina were enlarged. Spinal fusion was performed in three patients.

Of the 39 patients, 1 died postoperatively; 8 slowly worsened, 3 of whom died of intercurrent disease; the condition of 8 remained stationary, 1 of whom died of intercurrent disease; 9 showed slight improvement, 1 of whom died of intercurrent disease, and 13 improved considerably. Most of the patients who improved were in the younger age group.

ECHOLS, New Orleans.

Peripheral and Cranial Nerves

AMYLOID POLYNEUROPATHY. JOHN F. SULLIVAN, THOMAS E. WITCHELL, GHERARDO J. GHERARDI, and WILLIAM VANDER LAAN JR., Neurology 5:847 (Dec.) 1955.

Primary amyloidosis is a disease of mesenchymal tissue, whereas secondary amyloidosis affects parenchymatous organs. It is this predilection for involvement of mesenchymal tissue that enables one to establish a diagnosis of amyloid polyneuropathy, and previous observers have found the heart and larynx to be frequently involved in primary amyloidosis.

The authors report three cases of polyneuropathy due to primary amyloidosis in patients aged 50, 54, and 59. In each case a change in voice or clinical evidence of heart disease preceded the onset of the neuropathy. The neuropathy itself always began with involvement of the lower extremities, and burning pain in the soles was a prominent symptom. The involvement was asymmetrical at onset, but later equal involvement of the upper and lower extremities was found. Weakness and atrophy were most pronounced distally, and a marked disturbance in all modalities of sensation was noted in these areas.

Biopsy specimens of the peripheral nerves in two cases revealed the presence of amyloid deposits in the perineurium with the Congo red stain, whereas repeated peripheral nerve biopsy specimens in the third case showed no amyloid deposits in the peripheral nerve. A biopsy of the vocal cord, however, revealed a typical distribution of amyloid, which stained weakly with Congo red.

The difficulty of establishing a diagnosis of amyloid polyneuropathy had been noted by other observers, and the authors stress that repeated peripheral nerve biopsies may be negative with the Congo red stain. However, such a diagnosis can be made if there is involvement of the heart or larynx.

MANDEL, Philadelphia.

Encephalography, Ventriculography and Roentgenography

THE MYELOGRAPHIC APPEARANCE OF SACRAL CYSTS. WILLIAM B. SEAMAN and LEONARD T. FURLOW, J. Neurosurg. 13:88 (Jan.) 1956.

The origin and cause of sacral cysts are not clear, but it is thought that they arise from a splitting of the nerve root sheath, with distention of the potential space between endoneurium and perineurium to form a cyst. They occur most frequently on the second or third sacral root at the junction of the posterior root and dorsal ganglion.

The authors report the appearance of sacral cysts with myelography in four patients. There was thinning of the bone surrounding the sacral canal, usually at the second, third, and fourth sacral segments, which was readily demonstrated by lateral views of the sacrum. Myelography revealed a deformity of the lower end of the thecal sac, and in three of the four cases the cyst filled with the contrast media, indicating a communication with the subarachnoid space. In the fourth case, where no communication with the subarachnoid space existed, there was a lateral displacement of the cul-de-sac.

From a clinical standpoint, these cysts may be asymptomatic or may be associated with low-back pain. It is likely that cysts which do not communicate with the subarachnoid space may cause symptoms, for as they enlarge they become tense and press upon adjacent nerves.

MANDEL, Philadelphia.

UNILATERAL CALCIFICATION OF THE CHOROID PLEXUS IN A CHILD. J. G. TEPLICK and B. P. ADELMAN, Radiology 66:231 (Feb.) 1956.

Teplick and Adelman report the case of a child for whom roentgenograms of the skull were made because of trauma to the head. The roentgenograms showed no fracture of the skull, but a collection of small stippled calcifications, measuring about 1 cm. in diameter, was seen deep in the right parietal area. The location was typical for calcification in the glomus of the choroid plexus. However, since the calcification was unilateral and had occurred in a child, it was regarded with suspicion, and the child was examined carefully clinically for evidence of brain tumor. No such evidence was found, and additional special radiographic procedures were not carried out. The child was followed for two years by periodic neurological examination. Another roentgenogram of the skull after two years showed that the calcification was unchanged in size, but that it had become denser in appearance and that a smaller calcification in the region of the glomus of the left choroid plexus now had appeared. The case was considered unusual because

calcification in the glomus of the choroid plexus, while fairly common in the adult, is relatively rare in children. When calcification is present, either in children or adults, it is almost always bilateral and symmetrical.

WEILAND, Grove City, Pa.

CRANIAL MANIFESTATIONS OF FAMILIAL METAPHYSEAL DYSPLASIA. P. A. MORI and J. F. HOLT, Radiology 66:335 (March) 1956.

Mori and Holt report three cases of familial metaphyseal dysplasia (Pyle's disease), all of which had cranial abnormalities that have been described before by Neuhauser and others and that frequently accompany the characteristic changes seen in the long bones.

The diagnosis of familial metaphyseal dysplasia depends upon the roentgen finding of splayed long bones. When this splaying is found, familial metaphyseal dysplasia must be differentiated from bone marrow infiltration, deficiency states, developmental abnormalities, and toxic phenomena, all of which can produce the splaying.

The characteristic changes in the cranium consist of diffuse symmetrical hyperostosis of the skull and of the mandible with associated hypertelorism and obliteration of the paranasal sinuses. Encroachment of bone upon the neural foramina may produce blindness and other cranial nerve deficiencies. The changes in the skull are similar to those seen in patients with the diffuse symmetrical type of leontiasis ossea. When the latter disease is suspected, it is worth while to obtain films of the long bones to look for splaying.

WEILAND, Grove City, Pa.

News and Comment

ANNOUNCEMENTS

The Sixth International Neurological Congress.—The Sixth International Neurological Congress will be held in Brussels from July 21 to 28, 1957, in connection with the First International Congress of the Neurological Sciences.

The officers of the Congress are as follows: honorary presidents: Sir Gordon Holmes, Prof. Georges Guillain, Dr. Andre-Thomas, Prof. Th. Alajouanine, Prof. Antonio Flores, Prof. G. Monrad-Krohn, Dr. Knud Krabbe, Prof. Henry Alsop Riley, and Prof. P. Divry. Active officers: Prof. P. van Gehuchten, president; Dr. R. A. Ley, first vice-president; Dr. Ludo van Bogaert, secretary-general; Dr. J. Radermecker, assistant secretary-general; Dr. J. Titeca, treasurer, and Dr. R. A. Ley, editor of the *Transactions*.

At the time of the meeting of the Sixth International Neurological Congress, in Brussels, the following additional Congresses will be held: International League Against Epilepsy; First International Congress of Neurological Surgery; Third International Congress of Neuropathology; Fourth International Congress of Electroencephalography and Clinical Neurophysiology, and Fifth Symposium Neuroradiologicum.

The first day of the First International Congress of the Neurological Sciences, Sunday, July 21, will be devoted to (1) registration at the bureau of the Congress; (2) the official meeting of the International League Against Epilepsy, in the morning; (3) the plenary opening session of the Congress, in the afternoon, and (4) the formal reception for all participants of the Congress, in the evening.

Monday and Tuesday (July 22-23) will be devoted to reports and discussions concerning the two main topics common to all disciplines (neurology, neurosurgery, neuropathology, neuroradiology, electroencephalography, and clinical neurophysiology): (1) Extrapyramidal Pathology, the program of which will be organized by Prof. R. Garcin, France; and (2) Significance and Interpretation of Modifications of the Conscious State, the program of which will be organized by Prof. Geoffrey Jefferson, England.

Wednesday morning will be devoted to the main topic of the International Neurological Congress, namely, Multiple Sclerosis, the program for which will be organized by Dr. H. Houston Merritt, U. S. A., the afternoon being assigned to the main topic of the Congress of Neuropathology, namely, Pathologic Aspects of Multiple Sclerosis.

Thursday morning will be devoted to the main topic of the Congress of Electroencephalography and Clinical Neurophysiology; the afternoon, to the main topics of the Congress of Neurological Surgery, associated with the Symposium Neuroradiologicum: (1) Supratentorial Angiomas, and (2) Therapeutic Applications of Hypothermia.

Friday and Saturday will be devoted to miscellaneous communications and minor topics.

On Sunday, July 28, there will be (1) separate administrative meetings of the various disciplines; (2) a common administrative meeting of the representatives of the various disciplines in order to decide on the site of the Second International Congress of the Neurological Sciences, and (3) a celebration of the Centenary of Arthur van Gehuchten's birth, to be held in Louvain, Sunday afternoon.

The topics chosen by and the programs arranged for the International Congresses of Neurological Surgery, Neuropathology, Electroencephalography and Clinical Neurophysiology, the International League Against Epilepsy, and the Symposium Neuroradiologicum will be chosen by the respective committees in accordance with the criteria decided upon and will be publicized by these various organizations.

The program committees of the associated Congresses will arrange their own detailed programs: the Congress of Neuropathology, under the direction of Dr. Ludo van Bogaert; the Congress of Electroencephalography and Clinical Neurophysiology and also the International League Against Epilepsy, under the direction of Dr. J. Radermecker; the Congress of Neurological Surgery, under the direction of Dr. Brihaye (Brussels), and the Symposium Neuroradiologicum, under Prof. Melot (Brussels).

All of the associated Congresses will organize individual programs representing their several separate interests. The greatest emphasis will be placed upon subjects which will be of interest to all members of the Congress. Sessions for the presentation of miscellaneous

communications will be arranged for but are to be restricted in number, and they will be, so far as possible, grouped in appropriate subdivisions. In connection with these miscellaneous sessions devoted to individual communications, each national committee shall pass upon the desirability of admitting proposed contributions to the program, and final acceptance of the proposal will be made by action of the executive committee. Each member will be entitled to present only one communication in which his name appears as an author. At least one of the authors of each communication will be obligated to be present at the Congress to present the communication. Any author failing to present his communication before any session of the Congress will not be entitled to participate in future Congresses. Titles and summaries (not to exceed 250 words) of communications offered for presentation at the Sixth International Neurological Congress must be in the hands of the Secretary of the Committee for the United States, Dr. Pearce Bailey, National Institutes of Health, Bethesda 14, Md., before Feb. 1, 1957. No presentation will be placed on the program of the Congress unless the author has registered as a member of the Congress.

The membership of the Congresses shall consist of active, associate, and auxiliary members. The fee for active membership will be $15. Physicians in fields other than those represented by the individual congresses constituting the Congress of the Neurological Sciences are eligible for associate membership. The fee for associate membership will be $10. Nonmedical persons, such as members of families and others interested in the Congresses, will register as auxiliary members. The fee for such membership will be $5.

Application blanks for any type of membership in the Sixth International Neurological Congress or the Third International Congress of Neuropathology may be obtained by writing to the Secretary of the Committee for the United States, Dr. Pearce Bailey, National Institutes of Health, Bethesda 14, Md. Each applicant for active membership must be a member or present endorsement by some national or recognized local neurological, psychiatric, or neuropathologic organization.

Application blanks for membership in the First International Congress of Neurological Surgery may be obtained from the secretaries of the several neurosurgical societies in the United States. Application blanks for membership in the Fourth International Congress of Electroencephalography and Clinical Neurophysiology may be obtained from Dr. R. G. Bickford, Mayo Clinic, Rochester, Minn.

Thomas Cook & Son, Inc., and the American Express Company have been appointed as official travel agencies for the Congresses.

The Academy of Psychoanalysis.—At an organizational meeting in Chicago, on April 29, 1956, the Academy of Psychoanalysis was founded for the following purposes, as specified in its constitution:

The aims of the Academy are as follows: (*a*) to develop communication among psychoanalysts and their colleagues in other disciplines in science and in the humanities; (*b*) to constitute a forum for free inquiry into the phenomena of individual motivation and social behavior; (*c*) to encourage and support research in psychoanalysis; (*d*) to foster the acceptance of psychoanalysis and its integration in universities; (*e*) to advance the interests of psychoanalysis in all other respects.

The following officers were elected at the first meeting of the Academy: Janet MacKenzie Rioch, M.D., New York, president; Jules Masserman, M.D., Chicago, president-elect; Frances S. Arkin, M.D., New York, secretary; Leon Salzman, M.D., Washington, D. C., treasurer. Trustees: Nathan Freeman, M.D., Brooklyn; Frieda Fromm-Reichman, M.D., Washington, D.C.; Robert G. Heath, M.D., New Orleans; Elizabeth Kilpatrick, M.D., New York; John A. P. Millet, M.D., New York; William V. Silberberg, New York; Herbert Spiegel, M.D., New York; Clara Thompson, M.D., New York.

Physicians who are graduate psychoanalysts may qualify as Fellows. Physicians and others in related fields of behavior study may apply for acceptance as scientific associates. Meetings will occur semiannually. Communications to the Academy for Psychoanalysis may be addressed to the secretary or to any of the other officers.

Section on PSYCHIATRY

Reserpine in Hospitalized Psychotics

A Controlled Study on Chronically Disturbed Women

ARTHUR LEMON ARNOLD, M.D., Albuquerque, N. Mex.
and
HARRY FREEMAN, M.D., Worcester, Mass.

A voluminous literature has accumulated on the efficacy of reserpine in mental disorders, particularly in psychoses accompanied by uncontrolled behavior. As yet few reports have included double-blind controls with a published breakdown of the specific areas of clinical change. Hollister * found the dosage to be the most influential factor in a series of studies using varied doses, with the results expressed in terms of hospital adjustment. Hoffman and Konchegul,[3] Campden-Main and Wegielski,[4] and, more recently, Sommerness,[5] Forster,[6] and Cowden [7] reported similar studies.

The present study was intended primarily to determine an effective dosage of reserpine in chronic disturbed schizophrenic women, using a double-blind technique, for comparison with the effect of administering placebos and of giving no medication at all.

It was hypothesized that in adequate dosage reserpine will effect tranquilization of chronically disturbed psychotic women. In order to test this, it was necessary (1) to control the effects of suggestion on the patients, nurses, and physicians; (2) to control the reflection of general improvement in the ward environment onto the patients in the study, and (3) to record accurately many details of behavior.

Received for publication May 24, 1956.

From the Research Service, Worcester State Hospital.

Present Addresses: Lovelace Clinic, Albuquerque, N. Mex. (Dr. Arnold); Dementia Praecox Research Unit, Worcester State Hospital (Dr. Freeman).

* References 1 and 2.

Present Investigation

Experimental Design.—On the ward in which are treated the women who are the most disturbed (in terms of difficulty of hospital management—combative, destructive, denuditive, smearing, self-mutilative), those who were in psychotherapy or who were receiving electroshock therapy, who had had frontal lobotomies, or who consistently refused oral medications were excluded from the study but were retained on the ward. It was felt that results with lobotomized patients might not be applicable to patients whose brains were anatomically intact. Of more than 90 patients, all but 28 were thus excluded, and these 28 were studied (by the project observer, A. A.) for three weeks, after which ratings on a modified Malamud-Sands Worcester Rating Scale * were made of their behavior. Observations were thus systematically recorded for (1) neatness of appearance, (2) level of motor activity, (3) expressivity of face and gesture, (4) flexibility of responses, (5) control of hostility, (6) socialization (with disruptiveness and inaccessibility as extremes), (7) control of attention, (8) amount of speech, (9) level of mood, (10) quality and (11) demonstrability of feelings, (12) accuracy of perception, (13) logicality of thought, (14) defensive position (with omnipotence and nihilism as extremes), and (15) accuracy of self-evaluation. These 28 patients were then assigned (by the project administrator, H. F.) to one of three groups matched as to age, length of time since first hospitalization, and severity of disorder, as indicated by the base line rating scores. From Table 1 it may be seen

TABLE 1.—*Means and Ranges of Variables Used in Matching Patients for Reserpine, Placebo, and Nontreated Groups*

Variables	Reserpine		Placebo		Nontreated Group	
	Mean	Range	Mean	Range	Mean	Range
Age	44.6	23-66	52.2	34-67	44.3	29-58
Years in hospital	15.8	2-44	16.1	7 42	14.6	2-32
Baseline behavior score	50.0	17-73	50 5	27-75	44.8	28-69

that the matching was done rather accurately. One group, of 10 patients, was assigned to receive reserpine tablets; the second group, of 10, was designated to receive identical placebos, and the third group, of 8, was to receive no medication. The group to which any patient belonged was not known to the observer. For the duration of the study, no other therapy was given.

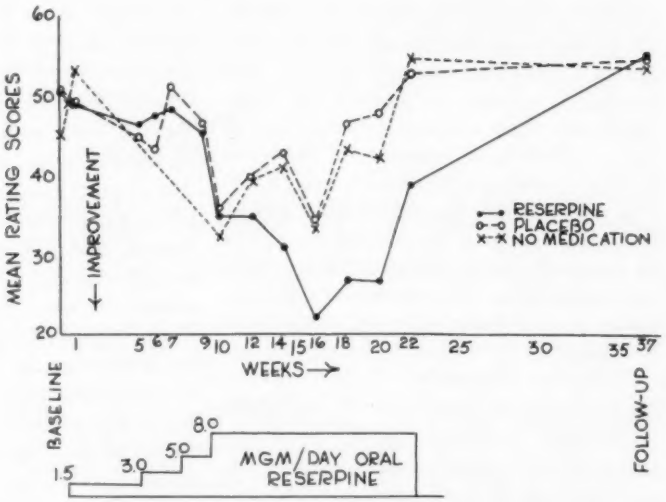
Method.—At intervals of approximately two weeks the observer recorded a behavior rating of each patient, in the scoring of which a numerical increase indicates greater abnormality. The reserpine dosage (all oral) was controlled by the administrator and was known only to him, the dose being the same for all patients in the reserpine group. At the start, 1.5 mg. of reserpine was given daily, and this was increased at 5 weeks to 3.0 mg., at 7 weeks to 5.0 mg., and at 9½ weeks to 8.0 mg., at which level it was continued for 13 weeks, when (in the 22d week of medication) the reserpine was discontinued.

Since the patients included in the study constituted less than a third of the ward population, and neither the nature of the medication nor a breakdown of the group was known to ward personnel, an atmosphere of pervasive and contagious enthusiasm, full of expectation of dramatic improvement, did not arise. The ward was not redecorated, and new, stimulating activities were not introduced into the ward routine. This was admittedly a stringent setting, but, as far as possible, factors related to "wonder drug" enthusiasm were avoided in an effort to measure drug effect alone as far as practicable.

Untoward Effects.—Several such effects in patients in the reserpine group caused some difficulty later in the assessment of the data. In the 11th week one patient, aged 66, developed sufficient orthostatic hypotension that she was transferred to the geriatric medical service by the ward physician, and reserpine was discontinued. Another patient, aged 55, developed mild congestive heart failure with moderate ankle edema at the conclusion of the study and required bed rest for a week to regain cardiac compensation; a similar situation has been reported by Perera.[9] A third patient, aged 57, frequently inactive, developed sudden signs of bowel obstruction and died just before going to surgery, in the 17th week of the study; autopsy findings did not rule out fecal impaction. Another patient, originally assigned to the reserpine group, refused all medication from the start and was transferred by the administrator to the control group which received no medication. Only one expected side-effect occurred, in which case a 29-year-old patient in the reserpine group developed Parkinsonian tremors at the conclusion of the study, but this was mild and was not present a week after the medication period.

Results.—There was no significant difference between the mean of the group receiving placebos and the mean of the group receiving no medication. Further, there were no significant differences between the means of these two control groups and that of the reserpine group until after the 10th week, when the reserpine dose had been increased to 8.0 mg. daily. It should be noted that only the divergent trends between the groups, rather than the absolute levels of the ratings, are pertinent, since the latter fluctuated over the period of the study, and it can be seen that whatever factors were operating affected all three groups in the same direction. The mean rating scores of the placebo and nontreated groups were in the direction of improvement on 8.0 mg. daily and continued as a trend for 10 weeks, but in the final 2 weeks of medication this divergence decreased (Figure). When the follow-up observations were recorded 15 weeks after medication was discontinued, the mean score of all groups had returned to the base line level.

Statistical Analysis (Table 2).—Those who received reserpine showed significant improvement in socialization, control of hostility, flexibility of responses, level of mood,



Clinical course of reserpine and control groups.

TABLE 2.—*Significance of Changes in Ratings for Individual Items in Rating Scale for Reserpine Patients Between a Four-Week Period on 3.0 and 5.0 Mg. Dosage and a Five-Week Period on 8.0 Mg. Dosage, and for the Placebo Patients Between the Same Periods; and Significance of Comparisons of the Changes in the Two Groups for Each Item*

Item	Reserpine (N=7)		Placebo (N=10)		Reserpine *vs.* Placebo
	Change	*P* Value	Change	*P* Value	*P* Value
Neatness of appearance	24	---	−12	---	
Level of motor activity	33	---	10	---	
Expressivity of face and gesture	29*	0.05	20	---	
Flexibility of responses	47*	0.02	23	---	
Control of hostility	50*	0.02	37*	0.02	
Socialization	48*	0.02	1	---	0.05†
Control of attention	33	---	− 6	---	
Amount of speech	25*	0.05	− 5	---	
Level of mood	45*	0.02	30	---	
Quality of feelings	35*	0. 5	38	---	
Demonstrability of feelings	40*	0.05	40*	0.02	
Accuracy of perceptions	42	---	35	---	
Logicality of thought	−1	---	−30	---	
Defensive position	41*	0.05	43*	0.01	
Accuracy of self-evaluation	−3	---	−81	0.01‡	

* Differences within reserpine and within placebo group are statistically significant by Wilcoxon's test for paired replicates.
† Differences between corresponding values in reserpine and placebo groups are statistically significant by the Mann-Whitney *u* test.
‡ Significantly worse to the 0.01 level of confidence.

expressivity of face and gesture, amount of speech, quality and demonstrability of feelings, and defensive position. Those who received placebos improved significantly in defensive position, control of hostility, and demonstrability of feelings and worsened significantly in accuracy of self-evaluation (perhaps only relatively, reflecting increased

familiarity with the patient). As a whole, all rating items considered, the reserpine group showed improvement greater than that of the placebo group which was statistically significant to the 0.05 level of confidence. The only aspect of behavior, however, showing improvement in the reserpine group which was significantly greater than that shown by the placebo group (by an extremely conservative statistical test [10]) was socialization; five reserpine-treated patients showed remarkable improvement in this respect.

Illustrative Responses.—Certain individual responses are illustrative of the effects noted above. Patient 1, age 30, denuditive, smearing, and apathetic, had been hospitalized six and one-half years and had had electroshock treatments during her first year in the hospital. Her base line rating score was among the worst in the reserpine group. After about two weeks on 8.0 mg. daily she was dressed, attentive, and able to communicate verbally. Improvement in this regard continued, reaching a peak 4 weeks later, but declined thereafter until, after 12 weeks on the same dosage, she was bizarre in her dress, deluded, and hallucinated, and was again unable to communicate her thoughts clearly. At the follow-up, less than four months after reserpine was discontinued, she was essentially the same as at the beginning of the study.

Another patient in the reserpine group, Patient 9, age 23, hospitalized seven years, was hallucinated and grimacing, combative, and explosive in her reactions at the start, and showed an unsteady, but marked, improvement in her control of assaultive and destructive behavior, with appropriate and pleasant expression and clarity of thought, after having received 8.0 mg. of reserpine daily for two weeks. She was even able to help serve meals to bed patients in an adjacent ward. After 12 weeks on this dosage, however, she was again so out of control that she enucleated her own eye.

A patient in the placebo group, Case 13, age 47, hospitalized over 10 years, was intensely preoccupied, pacing restlessly, constantly picking at her skin, and virtually uncommunicative. While there were slight fluctuations in her ability to respond meaningfully, her condition remained essentially unchanged throughout. Another placebo patient, Case 15, age 49, hospitalized over 20 years, was explosive, noisy, and socially disruptive, and had received without benefit pentylenetetrazol U. S. P. (Metrazol) convulsive therapy, hydrotherapy, and electroshock therapy. Near the end of the study she became calmer and was under adequate control nearly all the time except while dining in the cafeteria; there was no reversion to the initial abnormal level at the time of follow-up.

One of the patients who received neither reserpine nor placebos, Case 28, age 37, hospitalized over 10 years, with no satisfactory response to two courses of electroshock therapy, was hallucinating, silly, and bizarre in dress when the study began. By the 16th week she was still quite dependent and her expression was awkwardly exaggerated, but she was calm and more controlled. Eight weeks later, however, she again showed considerable scattering and was silly and aloof.

Summary

The data obtained may be summarized as follows:

1. No difference between the reserpine group and the placebo group appeared in the 28 chronically disturbed psychotic women until 8.0 mg. of reserpine was administered daily.

2. The placebo group did not differ from the group who were given no pills.

3. On the basis of an analysis of the scores on the individual items of a psychiatric rating scale, reserpine in adequate dosage was found to produce statistically significant improvement in socialization as compared with a placebo, but no other items showed improvement which was within the 0.05 level of confidence.

4. Great variation in amount and duration of improvement occurred, so that no patients were well enough to be discharged and all who had improved relapsed partially while receiving the same amount of reserpine, suggesting an escape from the medication effect.

5. Fifteen weeks after medication was discontinued, the mean rating scores of all three groups had returned to the base line level of abnormality.

Reserpine (Serpasil) and placebos were furnished through the courtesy of Ciba Pharmaceutical Products, Inc., Summit, N. J.

REFERENCES

1. Hollister, L. E.; Kreiger, G. E.; Kringel, A., and Roberts, R. H.: Treatment of Chronic Schizophrenic Reactions with Reserpine, Ann. New York Acad. Sc. 61:92 (April 15) 1955.

2. Hollister, L. E.; Traub, L., and Beckman, W. G.: Psychiatric Use of Reserpine and Chlorpromazine: Results of Double-Blind Studies, American Association for Advancement of Science, Publication No. 42, 1956.

3. Hoffman, J. L., and Konchegul, L.: Clinical and Psychological Observations on Psychiatric Patients Treated with Reserpine: A Preliminary Report, Ann. New York Acad. Sc. 61:144 (April 15) 1955.

4. Campden-Main, B. C., and Wegielski, Z.: The Control of Deviant Behavior in Chronically Disturbed Psychotic Patients by the Oral Administration of Reserpine, Ann. New York Acad. Sc. 61:117 (April 15) 1955.

5. Sommerness, M. D., and others; A Controlled Study of Reserpine on Chronically Disturbed Patients, A. M. A. Arch. Neurol. & Psychiat. 74:316 (Sept.) 1955.

6. Forster, W.; Schlichther, W., and Henderson, A. L.: Reserpine in Chronic Psychoses, Canad. M. A. J. 73:951 (Dec. 15) 1955.

7. Cowden, R. C.; Zax, M., and Sproles, J. A.: Reserpine: Alone and as an Adjunct to Psychotherapy, A. M. A. Arch. Neurol. & Psychiat. 74:518 (Nov.) 1955.

8. Malamud, W., and Sands, S. L.: A Revision of the Psychiatric Rating Scale, Am. J. Psychiat. 104:231 (Oct.) 1947.

9. Perera, G. A.: Edema and Congestive Failure Related to Administration of Rauwolfia Serpentina, J. A. M. A. 159:439 (Oct. 1) 1955.

10. Walker, H. M., and Lev, J.: Statistical Inference, New York, Henry Holt & Co., Inc., 1953.

The Psychopath in a Mental Institution

S. K. EHRLICH, M.D.
and
R. P. KEOGH, R.T., North Battleford, Sask., Canada

This study attempts to elucidate two questions:

1. What are the characteristics of those psychopaths who find their way to a mental institution?

2. What is the clinical difference between the psychopaths with a normal brain wave pattern and those who have an abnormal electroencephalogram?

The century-long nosological struggle with these troublesome people has left semantic scars on medical thinking (Bromberg [9]). Neither cake nor the whip produces any visible effect on their maladjustment (Bleuler [6]). Although essentially not different, they have just disharmony enough to be misfits in life.[79] We find among them Casanova and Don Juan, the morally insane [22] and the moral imbeciles,[70] the pathetically morbid[16] and the lucid melancholics,[72] the reasonable fools [72] and the reasoning phrenasthenics [91] of old writers. We find the criminaloid of Lombroso,[68] the constitutionally inferior of Adolph Meyer,[56] the psychopathic personality of Koch [86] and the creative psychopath of Henderson [43] the nomad of Rosanoff,[94] the anethopath of Karpman,* the perverse character of Menninger,[76] the sociopath of Kahn,[51] and the rebel without a cause of Lindner.[66] We come across the concept of anomia, of Rush [39]; the fate neurosis, of Alexander [3]; a phallic fixation, of Wittels [112]; the pathological personality, of Partridge [86]; the semantic disorder, of Cleckley [13] a loss of dimension, of Bender.[5] These difficult people display a primary affect hunger,[90] a deficiency in role playing,[36] a lack of crystallized experience,[83] and a psychogenic, acathexia.[90] They have been described as morally insensible,[71] morally atrophic,[62] instinct-ridden characters [29]; atavistic throwbacks [80]; homeostatically disturbed [67] and essentially inhuman [57]; egotropic [78]; evolutive anachronisms [52]; psychologically,[43] socially,[104] and electroencephalographically immature.[47] Therefore, to be generally understood, we still have to use the term "psychopath," introduced in English in 1847.[10]

A sociofugal attitude (Bromberg [9]) certainly does not help in the clarification of this concept, which remains largely an enigma.[72] The psychopaths are unquestionably ill,[17] and it may be valuable to single out from the many varieties of psychopathic personality a particular type or group.

Only very few objective facts stand out in the sea of confusion surrounding the concept of psychopathic personality. The brain wave pattern is such a fact. This pattern cannot be disguised or falsified. It does not depend on conscious direction. However little we know as yet about it, nobody doubts that it must have a meaning. The question is: How does it correlate with other personality features?

In an endeavor to find as many correlations as possible, we submitted to a clinical, psychometric, and statistical analysis altogether 50 factors, i. e., for age, 1; sex, 1; mode of admission, 3; background, 4; history, 4; attitude toward sex, 4; chronic suicide syndrome, 5; symptomatology, 10; diagnosis and prognosis, 2; EEG, 7 (nor-

Received for publication May 21, 1956.

Assistant to the Superintendent, Saskatchewan Hospital (Dr. Ehrlich).

EEG Technician, Saskatchewan Hospital, (Mr. Keogh).

* References 54, 55.

mal, 1, abnormal, 6); psychometrically measurable attitudes, 9.

Case Material

All our psychopaths were treated in a mental hospital. They had to display most of 10 symptomatological characteristics. They were diagnosed as psychopaths either plainly (pathological personality) or euphemistically (character neurosis), but with the elimination of brain pathology, epilepsy, major psychosis, or obvious psychoneurosis. They had to be physically healthy, electroencephalographically examined, and of sufficient intelligence to be psychometrically tested (MMPI). Their awareness of their identity had to be clear and free from any evidence of somatopsychic duality.[107] Ample biographical data had to be available.

We accumulated for this study a group of 50 patients, 38 men and 12 women. With the growing collection of data, it became apparent that, although the group as a whole had certain common features, a dividing line had to be drawn between 40 patients with an abnormal EEG and 10 without cerebral dysrhythmia. This ratio of 4:1 did not result from selection or coincidence. It corresponds with the over-all number of psychopaths who were admitted to the hospital throughout the last five years but whose records have not been included in this survey, as they did not meet all the required technical criteria.

Diagnostic Criteria

In our endeavor to cover the field and to make it as clear as possible with whom we were dealing, we selected for the purpose of clinical diagnosis the following 10 symptomatological syndromes:

1. Resentment. Resentment has its origin in an unadmitted inferiority or insufficiency (Brachfield[8]). The importance of feelings of inferiority in the personality pattern of the psychopath has been emphasized by other authors.†

2. Specialty: Parasitism (Karpman[54]; Cobb.[14])

3. No concept of time. Failure or inability to make practical use of the concept of time (Nielsen-Thompson[81]); arrested development in this field[95]; delight in dissipating time (Cohen[15]).

4. Semantic disorder. Personality so damaged that experience as a whole cannot be grasped or utilized in its ordinary significance or meaning.‡

5. No relationship capacity. No ability to invest relationships and thoughts with feeling and significance (Karpman[56]).

6. Lack of goal. No capacity for social striving, perseverance, and concentrated endeavor (Freyhan[31]).

7. Center of the universe. It is the patient's inner balance of affective and instinctive urges of the moment that determine his behavior, rather than the actual situation in which he finds himself (Sprague[103]).

8. Malformation of conscience. Faults in unconscious conscience formation resulting from disorders in the processes of introjection and identification (Glover[33]).

9. Disparity of the different qualities of personality. Mechanisms for monitoring or controlling behavior absent or inefficient.§

10. Low frustration tolerance. "Are we then at the mercy of these theta rhythms? Do they provide an excuse for outbursts of uncontrollable temper?" (Grey Walter[108]).

Age

Psychopaths with cerebral dysrhythmia show the tendency to come for treatment to a mental institution more frequently, and also at an earlier age, than the psychopaths with a normal EEG. Of the first group, 92.5% were under the age of 40, and so were 80% of the second group. We found no patient for this study above the age of 50. The psychopath apparently ceases to be a problem around the age of 45, or at least becomes a less conspicuous one.[25]

TABLE 1.—*Abnormality of EEG in Relation to Age*

Age	EEG Abnormal	EEG Normal
Under 20	22.5%	0.0%
21-30	37.5%	50.0%
31-40	32.5%	30.0%
41-50	7.5%	20.0%

†References 5, 22, 59, 84, 105, 109.

‡ References 13, 36, 50.

§ References 59, 1, 4, 77, 93.

TABLE 2.—*Incidence of EEG Abnormality in Relation to Mode of Admission*

Mode of Admission	EEG Abnormal	EEG Normal	Average Distribution of All Patients Admitted in 1951-1955
Voluntary	32.5%	20.0%	24.3%
Certified as mentally ill	35.0%	50.0%	72.9%
Judicial warrant	32.5%	30.0%	2.8%

Mode of Admission

The psychopath with cerebral dysrhythmia comes to the hospital more frequently of his own accord than the average mental patient (ratio about 3:2). The psychopath with normal brain waves comes for treatment more seldom of his own free will; he has to be certified in half the cases to come in at all. Both groups arrive with judicial warrants almost 12 times as frequently as the average mental patient.

Background

It appears from the data presented above that the EEG abnormal psychopaths have a higher incidence of early physical trauma in their history than the psychopaths with normal EEG's. Their sexual adjustment is closer to normal, with the struggle from adolescent experimenting to sexual maturity plainly apparent.

The EEG-normal psychopaths have a low incidence of early physical trauma but a higher frequency of psychogenic factors, such as faulty identification models,‖ broken homes, poor symbiosis with parents,[24] and delinquent integration.[7] They are older, but they display a strong tendency toward sexual aloofness or homosexual deviation, with only a fraction of them actually, at least superficially, sexually adjusted.

No statistically significant differences have been established between the male and the female patients in any of the correlations analyzed in this group.

The historical data concerning the overt behavior of the whole group are almost identical in the field of social maladjustment. The presence of psychopathic heritage, statistically high for the whole group (50%), seems to confirm the findings of other authors.¶

TABLE 3.—*Background, History, and Attitude toward Sex in Relation to the EEG*

History	EEG Abnormal	EEG Normal	Total
Background			
Psychopathic heritage	47.5%	60.0%	50.0%
Early physical trauma	50.0%	20.0%	44.0%
Faulty identification models	55.0%	80.0%	60.0%
Broken home	30.0%	40.0%	32.0%
History			
Rebelliousness	77.5%	70.0%	76.0%
Truancy and nomadism	70.0%	70.0%	70.0%
Distortion of judgment	95.0%	100.0%	96.0%
Social maladjustment	100.0%	100.0%	100.0%
Attitude toward sex			
Narcissistic	45.0%	70.0%	50.0%
Polysexual (57)	15.0%	0.0%	12.0%
Homosexual	5.0%	20.0%	8.0%
Heterosexual	35.0%	10.0%	30.0%

The Chronic Suicide Syndrome

The EEG-abnormal psychopaths appear to be more inclined to suicidal attempts and

‖ References 2, 5, 41, 93, 96.
¶ References 72, 101.

TABLE 4.—*The Chronic Suicide Syndrome in Relation to the EEG*

	EEG Abnormal	EEG Normal	Total
Suicidal attempts	22.5%	10.0%	20.0%
Accident proneness	45.5%	40.0%	44.0%
Addiction to drugs	12.5%	0.0%	10.0%
Alcoholism	67.5%	80.0%	70.0%
Delinquency	62.5%	80.0%	66.0%

to drug addiction, giving a malignant psychoneurotic coloring [111] to the first group. The EEG-normal psychopaths are rather prone to express their maladjustment by alcoholism and delinquency. However, even if delinquent, they are rather more painfully egocentric than deliberately destructive (Freyhan [31]).

The incidence of the definitely anomalous, self-thwarting,[11] hit-and-run,[98] self-destructive # accident proneness is almost equally high for the two groups (44%). It is an important factor, very interesting in these "people without conscience," and these "essentially inhuman parasites."

The correlation of this factor with age for the whole group gives us the data shown in Table 5. This curve for this correlation differs from other statistics (Dunbar [28]) based on other samples of the population. In this group it is not the rebellious adolescent who seeks self-destruction. In our study, it is the chronologically grown-up man, in trouble with authority throughout his life, who escapes into accident proneness from chronic resentment.

Symptomatology

Resentment, the impermeability to experience (Henderson [42]), selfishness, poor capacity for relationship, and the discrepancy between emotional and intellectual endowment are universal in the whole group. So is the low frustration tolerance, regardless of the EEG pattern. We have, however, to keep it in mind that susceptibility to frustration may be the sole observable remnant of anoxia,[12] a childhood disease,[38] or an early encephalopathy.*

TABLE 5.—*Age and Accident Proneness*

Age	Incidence of Accident Proneness
Under 20	9.1%
21-30	27.3%
31-40	50.0%
41-50	13.6%

The statistical frequency of pure parasitism is amazingly low in the whole group, but relatively somewhat higher in the EEG-normal group. The EEG-abnormal psychopaths have more trouble with the appreciation of time. The concept of malformation of conscience [53] apparently does not apply to every psychopath—a superego seems to be undoubtedly present, although "soluble in alcohol" (Fenichel [29]).

TABLE 6.—*Symptomatology in Relation to the EEG*

Symptoms	EEG Abnormal, %	EEG Normal, %	Total, %
Resentment	100.0	100.0	100.0
Parasitism	35.0	50.0	38.0
No concept of time	87.5	50.0	80.0
Semantic disorder	100.0	100.0	100.0
No relationship capacity	80.0	90.0	82.0
Lack of goal	90.0	100.0	92.0
Center of universe	100.0	100.0	100.0
Malformation of conscience	87.5	70.0	86.0
Disparity of qualities	100.0	100.0	100.0
Low frustration tolerance	100.0	100.0	100.0

Diagnosis and Prognosis

In the diagnostic and prognostic assessment of the psychopath, the clinician still has to use his own judgment, as he has no strictly objective data for his guidance. However subjective and variable this judgment happens to be, we find in our case material, nevertheless, a marked trend toward a severer and more pessimistic opinion in the clinical evaluation of illness and

References 3, 29.

* References 69, 81.

TABLE 7.—*Diagnosis and Prognosis*

	EEG Abnormal	EEG Normal	Total
Diagnosis			
Psychopath (pathological personality)	55.0%	70.0%	58.0%
Psychopath (character neurosis)	45.0%	30.0%	42.0%
Prognosis			
Fair	45.0%	10.0%	38.0%
Poor	55.0%	90.0%	62.0%

outlook of the EEG-normal than of the EEG-abnormal psychopath. Repeated admissions of some patients and later reports, when available, generally confirmed this trend and justified the judgment. In no case had the EEG alone or the present study any influence upon these factors.

Electroencephalographic Data

All the patients were examined at least once. The EEG recorder used was a Grass eight-channel Model 3B. The technique was the same for all patients. No sedation was administered. The patients were always fully conscious when examined.

Unipolar and bipolar runs were done, with the electrodes applied to the frontal, temporal, parietal, and occipital regions on both sides and to both ears. Hyperventilation was carried out for four minutes, as well as photic stimulation for short periods of time. There were no statistically significant differences between male and female patients in our material, confirming in this respect the findings of Hill,[47] as well as of Knott and Gottlieb.[60]

The incidence of cerebral dysrhythmia in our case material (80%) must be regarded as high. Although the EEG abnormalities usually found in psychopaths are in no way specific or diagnostic (Hill [48]), the incidence of the theta rhythm (4-7 cps) among the normal population is rare: 0.7%.[46] The bilateral synchronous paroxysmal slow activity has been associated by some authors with a tendency toward delinquent abreaction †; but, curiously enough, it seems to be rather a "homeostatic phenomenon," related not to the development of illness but to recovery from it (Hill [48]). This rhythm is not found in normal children.[48]

The four classes of phenomena—alpha variant (submultiple frequency of the alpha rhythm), excess theta, dominant theta, and a temporal slow-wave focus (postcentral)—have been interpreted as a failure of the maturational process,‡ a failure of the functional organization [89] and integration [47] of the cerebral cortex, with the involvement of various diencephalothalamic struc-

TABLE 8.—*Electroencephalographic Data*

Normal 10 patients (20%)			
Abnormal 40 patients (80%)			
Alpha variants	25/40	62.5%	
Bilateral synchronous paroxysmal slow activity	18/40	45.0%	
Excess theta rhythm	19/40	47.0%	
Dominant theta rhythm	18/40	45.0%	
Temporal slow wave focus			
Anterior	2/40	5.0%	(bilateral)
Middle and posterior	31/40	77.5%:	Bilateral: 50.0% Left : 22.5% Right : 5.0%

† References 82, 87.

‡ References 28, 45, 46, 47, 48, 65, 89.

tures.§ They may be understood as an apparent persistence of childhood patterns in adult life.‖ These abnormalities decrease with age.¶ The theta activity seems to disappear later on the left than on the right side.[92]

The temporal lobes show the highest development in man, as compared with that in lower animals.[47] Protected by a thin skull and crowded against a shelf of bone,[32] they are exposed to innumerable opportunities for minor developmental failure, which comes to light only when that part of the apparatus is called into use.# There is a high (50% in the material) correlation of dysrhythmia with an antecedent history of early trauma.* This correlation is actually probably higher: the severity and nature of a trauma is very different from the standpoint of the fetus than from its appraisal by an obstetrician (Sontag[102]). Young children live in a world which few of them can describe and few adults remember; the special features of this world determine, as much as anything else, the theta patterns of the young (Grey Walter[108]). We may recognize from the "slant and twist" which way the wind has blown (Williams[110]). The patient with even minor abnormalities of the EEG appears to be unduly sensitive to environmental stresses of all kind.†

The high incidence of psychopathic heritage (47.5%) in our data possibly may indicate the importance of genetic factors.‡

The Minnesota Multiphasic Personality Inventory

The MMPI § has been found in this study a clinically valuable test in the assessment of faulty attitudes toward the basic problems of survival. It facilitated also the study of correlations hardly measurable otherwise. All our tests had valid scores.

1. We found an abnormally elevated score for psychopathic deviation (Pd) in 28 EEG-abnormal patients (70%) but in all 10 of the EEG-normal group (100%), indicating perhaps that the psychopaths without dysrhythmia are generally more determined to adhere to their faulty attitudes, more outspoken in the expression of their deviant personality pattern. This finding, in connection with their clinically poor prognosis, appears to confirm strongly the conclusions of Levy and Kennard[64] in regard to the severity of their social maladjustment.

2. Quite paradoxically, an abnormally elevated Mf score (tendency toward masculinity or femininity of interest pattern) occurred in 11 of the EEG-abnormal patients (27.5%), indicating a neurotic dissatisfaction with their own sex, whereas in the EEG-normal group this elevated Mf score occurred only once (10%). Patients with a normal EEG appear to accept more easily and without rebellion the fact of being either male or female, even when not sexually normal or mature, whereas the EEG-abnormal group presents a real battlefield of emotional conflicts and burning resentment against the fact of having been mercilessly sentenced at birth to grow up as a male or a female.

3. The "Suicide Key": Elevated scores for depression and psychasthenia[100] occurred only twice, both times in the EEG-abnormal group, in spite of the history of actual serious suicidal attempts in the biography of 10 patients (EEG-abnormal, 9; EEG-normal, 1). This discrepancy may indicate that an attempt at self-destruction in a psychopath is motivated rather by a sudden impulse than by a depressive attitude, gradually increasing in intensity for a certain length of time and therefore apparent in this test.

4. The "Double-Spike" Pattern: Elevated scores for psychopathic deviation and mania[97] occurred only in the tests of three patients (all EEG-abnormal). The psycho-

§ References 20, 30.
‖ References 48, 49, 108.
¶ References 27, 34, 37, 47, 48.
# References 59, 81.
* References 27, 34, 48, 58, 59, 60.
† References 48, 58, 99.
‡ References 28, 30, 35, 48, 61.
§ References 40, 74.

paths who come for treatment to a mental institution seem to have less inclination to manic attitudes as compared with those who manage to avoid hospitalization.

Other scores on our MMPI records presented a broadly scattered pattern, valuable in the assessment of individuals but otherwise inconclusive.

Maladjustment, Disease or Personality?

This question, set by Karl Menninger in 1941,[75] still remains timely in the approach to the problem of the psychopathic personality. Applied to our data, it would result in a tentative conclusion that, although all psychopaths admitted to a mental institution present certain features characteristic of the whole group, there is a clinical difference between those with normal brain waves and those with cerebral dysrhythmia. Instability of personality and instability of EEG pattern coincide in many instances.[59]

In view of our findings the EEG-abnormal psychopath seems to suffer not from a "mythical"[85] but from a true illness,‖ a valid clinical entity,[87] neither purely "social" nor altogether "neurotic." He has a less-synthetized, a relatively weaker, ego than the neurotic,[88] from whom he differs[21] by his inability to grasp experience, his lack of self-control, his faulty attitudes—rebelliousness, truancy, delinquency, social maladjustment—his inability to utilize time, his low frustration tolerance, and his cerebral dysrhythmia. He has a high incidence of early physical trauma, and ultimately a well-defined organic etiology may be recognized as the cause of his illness.

The EEG-normal psychopath presents, rather, a personality pattern, deviant but stabilized, with the machinery for forethought available,[73] but also with a chronic resentment against the intrusion of any reality which challenges his illusion of omnipotence.[111]

Both the ill and the deviant suffer from a conflict revolving around a moral masochism.[9] Both require treatment which would utilize the positive values, undoubtedly present in every patient.[44] This treatment should be conducted in special settlements, isolating the psychopath in a culture of his own.¶ He is too expensive to be disregarded. Should any statistics in this field ever be computed, it would not be very surprising if the damage to society resulting from the general sociofugal[9] attitude toward this real and extremely serious disability[13b] would be expressed by higher figures than the cost of poliomyelitis or tuberculosis.

Conclusions

A group of 50 psychopaths admitted to a mental institution were studied by a correlation of clinical, biographical, symptomatological, electroencephalographic, and psychometric factors.

The psychopath with cerebral dysrhythmia (80%) comes for treatment frequently on his own accord and at a comparatively early age. He has a high incidence of early physical trauma. He is inclined to suicidal attempts and to drug addiction. He has difficulties with the concept of time. His sexual adjustment is closer to normal, but evidence of a struggle in this area is apparent in his attitudes. He shows signs of physiological immaturity and homeostatic disturbance in his brain wave pattern. He is socially maladjusted in his psychometric profile. He is ill, but his prognosis for ultimate recovery is not quite bad.

The psychopath with a normal EEG (20%) appears to be more deviant, but also more stabilized, in his anomalous personality pattern. He comes for treatment unwillingly and late. He has experienced a high incidence of harmful environmental factors. He is sexually aloof or perverted, but without much evidence of inner conflict in this field. He shows a marked trend toward delinquency and alcoholism. He is frequently a parasite. His measurable attitudes show a very high degree of social maladjustment, and his outlook is dubious.

‖ References 17, 18, 19, 42, 63.

¶ References 26, 106.

Rebelliousness, truancy, faulty judgment, resentment, impermeability to experience, selfishness, and a discrepancy between intellectual and emotional endowment, as well as low frustration tolerance, are universal in the whole group. So is the high incidence of psychopathic heritage. The whole group displays a considerable frequency of a chronic suicide syndrome, particularly a definitely self-destructive trend in accident proneness, startlingly high in those "people without conscience."

Dr. F. S. Lawson, Dr. D. G. McKerracher, and Dr. M. Demay gave criticism; the medical staff of our institution permitted use of their case material, and Mrs. S. Corrigall, Clinical Psychologist, did psychometric work and discussed the problem with us.

REFERENCES

1. Abrahamsen, D.: Motivation of Crime, J. Nerv. & Ment. Dis. 103:549, 1946.

2. Aichhorn, A.: Wayward Youth, London, Putnam & Co., Ltd., 1936.

3. Alexander, F., and Ross, H.: Dynamic Psychiatry, Chicago, University of Chicago Press, 1950.

4. Alvarez, W. C.: The Neuroses, Philadelphia, W. B. Saunders Company, 1951.

5. Bender, L.: A Dynamic Psychopathology of Childhood, Springfield, Ill., Charles C Thomas, Publisher, 1954.

6. Bleuler, E.: Textbook of Psychiatry, New York, The MacMillan Company, 1930.

7. Bloch, D. A.: The Delinquent Integration, Psychiatry 15:297, 1952.

8. Brachfield, O.: Inferiority Feelings in the Individual and the Group, London, Routledge & Kegan Paul, Ltd., 1951.

9. Bromberg, W.: The Treatability of the Psychopath, Am. J. Psychiat. 110:604, 1954.

10. Bunker, H. A.: Psychiatric Etymology, Am. J. Psychiat. 84:70, 1927.

11. Cason, H.: The Characteristics of the Psychopath, Am. J. Psychiat. 105:218, 1948.

12. Chornyak, J.: Diagnosis of Psychopathic Delinquents, Am. J. Psychiat. 97:1326, 1941.

13. Cleckley, H.: (*a*) The Mask of Sanity, Ed. 2, 1950; (*b*) Idem, Ed. 3, 1955, St. Louis, C. V. Mosby Company.

14. Cobb, S.: Foundations of Neuropsychiatry, Baltimore, Williams & Wilkins Company, 1952.

15. Cohen, J.: The Experience of Time, Acta psychol. 10:207, 1954.

16. Conn, J. H.: The Aggressive Female Psychopathic Personality, J. Nerv. & Ment. Dis. 95:316, 1942.

17. Cruvant, B. A., and Yochelson, L.: The Psychiatrist and the Psychotic Psychopath, Am. J. Psychiat. 106:594, 1950.

18. Darling, H. F.: Definition of Psychopathic Personality, J. Nerv. & Ment. Dis. 101:121, 1945.

19. Darling, H. F., and Sanddal, J. W.: A Psychopathic Concept of Psychopathic Personality, J. Clin. & Exper. Psychopath. 13:175, 1952.

20. Delafresnaye, J. F.: Brain Mechanisms and Consciousness, Springfield, Ill., Charles C Thomas, Publisher, 1954.

21. Diethelm, O.: Treatment in Psychiatry, Springfield, Ill., Charles C Thomas, Publisher, 1950.

22. Dorcus, R. M., and Shaffer, G. W.: Textbook of Abnormal Psychology, Baltimore, Williams & Wilkins Company, 1950.

23. Dunbar, F.: Psychosomatic Diagnosis, New York, Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1948.

24. Dunbar, F.: Symbiosis of Parent and Child, Am. J. Orthopsychiat. 22:809, 1952.

25. East, W. Norwood: Psychopathic Personality and Crime, J. Ment. Sc. 91:426, 1954.

26. Ehrlich, S. K.: The Psychopathic Personality, Sask. Psychiat. Serv. J. 2:17, 1955.

27. Ellingson, R. J.: The Incidence of EEG Abnormality Among Patients with Mental Disorders of Apparently Nonorganic Origin, Am. J. Psychiat. 111:263, 1954.

28. Feldmann, H.: L'Électro-encéphalogramme dans les troubles du caractère et du comportement chez l'enfant, Schweiz. Arch. Neurol. u. Psychiat. 69:170, 1952.

29. Fenichel, O.: The Psychoanalytical Theory of Neurosis, New York, W. W. Norton & Company, Inc., 1945.

30. Fontes, V.: Infantile Psychopathies and Aetiological Considerations: abstr., Excerpta med. VIII 5:1083, 1952.

31. Freyhan, F. A.: Clinical Evaluations of Psychopathic Personalities, Delaware M. J. 22:196, 1950.

32. Gibbs, F. A.: The Most Important Thing, Am. J. Pub. Health 41:1504, 1951.

33. Glover, E.: The Aetiology and Classification of Psychopathies, Proc. Roy Soc. Med. 47:638, 1954.

34. Gottlieb, J. S.; Ashby, M. C., and Knott, J. R.: Primary Behavior Disorders and Psychopathic Personality: 1. Correlations of the EEG with Family History and Antecedent Illness or Injury, Arch. Neurol. & Psychiat. 56:381, 1946.

35. Gottlieb, J. S.; Ashby, M. C., and Knott, J. R.: Studies in Primary Behavior Disorders and Psychopathic Personality: 2. The Inheritance of Electrocortical Activity, Am. J. Psychiat. 103:823, 1947.

36. Gough, H. A.: A Sociological Theory of

Psychopathy, in Mental Health and Mental Disorder: A Sociological Approach, Society for Study of Social Problems, A. M. Rose, Editor, New York, W. W. Norton & Company, Inc., 1955, Chap. 18.

37. Greenblatt, M.: Age and EEG Abnormality in Neuropsychiatric Patients, Am. J. Psychiat. 101:82, 1944.

38. Grinker, R. R.: The Effect of Infantile Disease on Ego Patterns, Am. J. Psychiat. 110:290, 1953.

39. Guttmacher, M. S., and Weihofen, H.: Psychiatry and the Law, New York, W. W. Norton & Company, Inc., 1952.

40. Hathaway, S. R., and McKinley, J. C.: Minnesota Multiphasic Personality Inventory Manual, Ed. 2, New York, The Psychological Corporation, 1951.

41. Heaver, W. L.: A Study of 40 Male Psychopathic Personalities Before, During and After Hospitalization, Am. J. Psychiat. 100:345, 1943.

42. Henderson, D. K.: Psychopathic States, New York, W. W. Norton & Company, Inc., 1947.

43. Henderson, D. K., and Gillespie, R. D.: Textbook of Psychiatry, London, Oxford University Press, 1950.

44. Heringa, S.: On the Treatment of Psychopaths, Folia psychiat. 53:806, 1950; Digest. Neurol. & Psychiat. 19:197, 1951.

45. Hill, D., and Watterson, D.: EEG Studies of Psychopathic Personalities, J. Neurol. Neurosurg. & Psychiat. 5:47, 1942.

46. Hill, D.: EEG in Episodic Psychotic and Psychopathic Behavior, Electroencephalogy & Clin. Neurophysiol. 4:439, 1952.

47. Hill, D.; Parr, G., and others: Electroencephalography, London, MacDonald & Co., Ltd., 1952.

48. Hill, D.: Electroencephalography, in Recent Advances in Neurology and Neuropsychiatry, W. R. Brain and E. B. Strauss, Editors, London, J. & A. Churchill, Ltd., 1955.

49. Hodge, R. S.: The Impulsive Psychopath: A Clinical and Electrophysiological Study, J. Ment. Sc. 91:472, 1945.

50. Johnson, W.: People in Quandaries, New York, Harper & Brothers, 1946.

51. Kahn, E.: Psychopathic Personalities, New Haven, Conn., Yale University Press, 1931.

52. Kahn, E.: Thoughts on Problems of Psychopathy, Monatsschr. Psychiat. u. Neurol. 118:242, 1949.

53. Karpman, B.: Criteria for Knowing Right from Wrong, J. Crim. Psychopath. 2:376, 1941.

54. Karpman, B.: Psychopathy in the Scheme of Human Topology, J. Nerv. & Ment. Dis. 103:276, 1946.

55. Karpman, B.: The Myth of Psychopathic Personality, Am. J. Psychiat. 104:523, 1948.

56. Karpman, B.: A Differential Study of Psychopathic Behavior in Infants and Children, Am. J. Orthopsychiat. 22:263, 1952.

57. Kavka, J.: Between Psychosis and Psychopathy, J. Nerv. & Ment. Dis. 106:19, 1947.

58. Kennard, M.: The EEG in Psychological Disorders, Psychosom. med. 15:95, 1953.

59. Kennedy, A.: Psychopathic Personality and Social Responsibility, J. Ment. Sc. 100:873, 1954.

60. Knott, J. R., and Gottlieb, J. S.: Evaluation of Psychopathic Personality, Arch. Neurol. & Psychiat. 52:515, 1944.

61. Knott, J. R.; Platt, E. B.; Ashby, N. C., and Gottlieb, J. S.: The Familial Evaluation of the EEG of Patients with Primary Behavior Disorder and Psychopathic Personality, Electroencephalog. & Clin. Neurophysiol. 5:363, 1953.

62. Kraepelin, E.: Lectures on Clinical Psychiatry; authorized translation from the German, revised and edited by Thomas Johnstone, Ed. 3, London, Baillière, Tindall & Cox, 1913.

63. Kraines, S. H.: The Therapy of Neuroses and Psychoses, Lea & Febiger, Philadelphia, 1948.

64. Levy, S., and Kennard, M.: A Study of the EEG as Related to Personality Structure in a Group of Inmates of a State Penitentiary, Am. J. Psychiat. 109:832, 1953.

65. Levy, S., and Kennard, M.: The EEG Pattern of Patients with Psychologic Disorders of Various Ages, J. Nerv. & Ment. Dis. 118:416, 1953.

66. Lindner, R. M.: Rebel Without a Cause, New York, Grune & Stratton, Inc., 1944.

67. Lindner, R. M.: Psychopathic Behavior, in Encyclopedia of Psychology, P. D. Harriman, Editor, New York, Philosophical Library, Inc., 1946.

68. Lombroso, C.: Crime: Its Causes and Remedies, translated by H. P. Horton, Boston, Little, Brown & Co., 1918.

69. Lurie, L. A.: Psychopathic Behavior of "Idiopathic" Origin, Am. J. Orthopsychiat. 21:225, 1951.

70. Maudsley, H.: The Pathology of Mind, London, Macmillan Co., 1895.

71. Maudsley, H.: Responsibility of Mental Disease, New York, D. Appleton & Co., 1900.

72. Maughs, S.: A Concept of Psychopathy and Psychopathic Personality, J. Crim. Psychopath. 2:329, 1941.

73. Mayer-Gross, W.; Slater, E., and Roth, M.: Clinical Psychiatry, London, Cassell & Co., Ltd., 1954.

74. McKinley, J. C., and Hathaway, S. R.: The Minnesota Multiphasic Personality Inventory: 5. Hysteria, Hypomania and Psychopathic Deviates, J. Appl. Psychol. 28:153, 1944.

75. Menninger, K. A., in discussion on Psychopathology of Psychopathic Personalities, Bull.

New York Acad. med. 17:911, 1941; J. Nerv. & Ment. Dis. 94:198, 1941.

76. Menninger, K. A.: Recognizing and Renaming Psychopathic Personalities, Bull. Menninger Clin. 5: 1951.

77. Michaels, J. J.: Delinquency and Control, Am. J. Orthopsychiat. 24:258, 1954.

78. Muncie, W.: Psychobiology and Psychiatry, St. Louis, C. V. Mosby Company, 1948.

79. Myerson, A.: The Inheritance of Mental Diseases, Baltimore, Williams & Wilkins Company, 1925.

80. Newkirk, P. R.: Psychopathic Delinquents, Dis. Nerv. System 14:52, 1953.

81. Nielsen, J. M., and Thompson, G. N.: The Engrammes of Psychiatry, Springfield, Ill., Charles C Thomas, Publisher, 1947.

82. Ostow, M., and Ostow, M.: Bilaterally Synchronous Paroxysmal Slow Activity in the EEG of Non-epileptics, J. Nerv. & Ment. Dis. 103:346, 1946.

83. Palmer, D. M., and Rock, H. A.: Brain Wave Patterns and "Crystallized Experiences", Ohio M. J. 49:804, 1953.

84. Partridge, G. E.: Psychopathic Personalities Among Boys in a Training School for Delinquents, Am. J. Psychiat. 85:159, 1928.

85. Partridge, G. E.: Psychotic Reaction in the Psychopath, Am. J. Psychiat. 85:493, 1928.

86. Partridge, G. E.: Current Conceptions of Psychopathic Personality, Am. J. Psychiat. 87, 53, 1930.

87. Penfield, W., and Jasper, H.: Epilepsy and the Functional Anatomy of the Human Brain, Boston, Little, Brown & Company, 1954.

88. Peto, A.: The Interrelations of Delinquency and Neurosis, Brit. J. M. Psychol. 27:1, 1954.

89. Pond, D. A.; Rey, J. H., and Hill, D.: Biological Correlates of Constitutional EEG: Abnormalities of the Temporal Lobes, Electroencephalog. & Clin. Neurophysiol. 2:111, 1950.

90. Rabinovitch, R. D.: The Concept of Primary Psychogenic Acathexia, Am. J. Orthopsychiat. 21:231, 1951.

91. Régis, E.: A Practical Manual of Mental Medicine, Utica, N. Y., American Journal of Insanity, 1894.

92. Rey, J. H.; Pond, D. A., and Evans, C. C.: Clinical and EEG Studies of Temporal Lobe Function, Proc. Roy Soc. Med. 42:891, 1949.

93. Rodgers, T. C.: A Dynamic Study of the So-Called Psychopathic Personality, J. Nerv. & Ment. Dis. 107:43, 1948.

94. Rosanoff, A. J.: Manual of Psychiatry, New York, John Wiley & Sons, Inc., 1927.

95. Schecter, D. E.; Symonds, M., and Bernstein, I.: Development of the Concept of Time in Children, J. Nerv. & Ment. Dis. 121:301, 1955.

96. Schmideberg, M.: Is the Criminal Amoral? Brit. J. Delinquency 4:272, 1954.

97. Schneck, J. M.: The Double Spike Pattern on the Minnesota Multiphasic Personality Inventory, Am. J. Psychiat. 104:443, 1948.

98. Selling, L. S.: The Psychopathology of the Hit-and-Run Driver, Am. J. Psychiat. 98:93, 1941.

99. Silverman, D.: Implications of the EEG Abnormalities in the Psychopathic Personality, Arch. Neurol. & Psychiat. 62:870, 1949.

100. Simon, W., and Hales, W. M.: Note on a Suicide Key in the Minnesota Multiphasic Personality Inventory, Am. J. Psychiat. 106:222, 1949.

101. Slater, E.: Heredity in Mental Disease, in British Encyclopedia of Medical Practice, edited by Sir Humphrey Rolleston, London, Butterworth & Co., Ltd., 1938, Vol. 8, p. 560, 1938.

102. Sontag, L. W.: Differential Etiological Factors in Psychopathic Behavior in Children, Am. J. Orthopsychiat. 22:224, 1952.

103. Sprague, G. S.: The Psychopathology of Psychopathic Personalities, Bull. New York Acad. Med. 17:911, 1941; Nerv. & Ment. Dis. 94:193, 1941.

104. Stalker, H.: Psychopathic Personality, in Modern Trends in Psychological Medicine, N. G. Harris, Editor, London, Butterworth & Co., Ltd., 1948.

105. Strecker, E. A.; Ebaugh, F. G., and Ewalt, J. R.: Practical Clinical Psychiatry, Philadelphia, The Blakiston Company, 1948.

106. Taylor, S.: The Psychopath in our Midst: A Danish Solution, Lancet 1:32, 1949.

107. Todd, J.: The Syndrome of Alice in Wonderland, Canad. M. A. J. 73:701, 1955.

108. Walter, W. Grey: The Living Brain, London, Gerald Duckworth & Co., 1953.

109. Weiss, E., and English, O. S.: Psychosomatic Medicine, Philadelphia, W. B. Saunders Company, 1949.

110. Williams, D.: Cerebral Basis of Temperament and Personality, Lancet 2:1, 1954.

111. Winkler, E. G.; Weissman, M., and McDermaid, G.: Alcoholism and Antisocial Behavior, Psychiat. Quart., Supp. 28, 242, 1954.

112. Wittels, F.: The Position of the Psychopath in the Psycho-Analytic System, Internat. J. Psycho-Analysis 19:471, 1938.

Psychologic Studies in Hypothyroidism

Recommendations for Case Management

JOHN MONEY, Ph.D., Baltimore

Introduction

The relationship between intellectual impairment and thyroid deficiency is far from being completely elucidated. Recent literature on the subject is not voluminous.* One may expect that many questions will continue to remain unanswered until the physiology and biochemistry of thyroid function and failure are more perfectly understood. Current limitations notwithstanding, one may also expect the evidence collected from a large, randomly selected sample of hypothyroid patients to shed some light on the relationship between cognitional dysfunction and thyroid dysfunction. For this reason, I have, during the past four years, kept a group of patients with a history of hypothyroidism under psychologic study and have given an intelligence test to each of 70 such patients.

Method of Investigation

For the 20 years between 1935 and 1955, the files of the pediatric-endocrine clinic of the Harriet Lane Home record 149 cases of hypothyroidism. A few of these patients are now dead. A few, probably no more than half a dozen, are permanently institutionalized mental defectives who have not returned to the hospital for years. Others live at long distances from the hospital, so that their return visits are sporadic or have lapsed. A large proportion of the total still returns to the clinic for follow-up study, from time to time.

In order to reduce statistical sampling biases to a minimum, patients to be given an intelligence test were randomly selected in three groups. The first group included all those patients with a history of hypothyroidism who returned to the pediatric-endocrine clinic of the Harriet Lane Home during the year 1952 for a routine follow-up examination. Some of these patients, of whom the oldest was 24, had been on thyroid substitution therapy for many years.

The second group enlarged the sample to include 47 patients and comprised those of the clinic's hypothyroid patients who were not scheduled for an endocrine follow-up in 1952 but whose homes were within a half-day's journey of The Johns Hopkins Hospital. They came to the hospital for an intelligence test.

The third group, comprising an additional 24 patients, raised the total number of cases to 70. These 24 patients were seen in the clinic during the four years from 1952 to 1955, inclusive; they constituted all of the new cases of hypothyroidism in the clinic, not previously diagnosed or treated elsewhere, who were 2 years old or older by the end of 1955. They were all tested after euthyroidism had been established, though those who were old enough had also been tested before commencement of thyroid treatment.

All of the patients who received their initial diagnosis and treatment in our clinic during the four years since this study began have been under psychologic surveillance, intermittently, while on treatment with desiccated thyroid. Their medication has been regulated by Dr. Lawson Wilkins, on the basis of both clinical and laboratory criteria, to keep them at the euthyroid level of hormonal functioning.[8] The usual procedure has been to begin with an initial dose of thyroid U. S. P. of ½ grain (30 mg.) daily with older children or ¼ grain (15 mg.) daily with very young children,

Received for publication April 20, 1956.

Department of Psychiatry, The Johns Hopkins University School of Medicine.

This study is part of a larger program of research in psychiatry and endocrinology supported by a grant from the Josiah Macy Jr. Foundation. The program is under the aegis of John C. Whitehorn, Professor of Psychiatry, The Johns Hopkins University, and of Lawson Wilkins, Associate Professor of Pediatrics, Acting Pediatrician-in-Chief, director of pediatric endocrinology at The Johns Hopkins Hospital. The study in hypothyroidism has been conducted with the active collaboration of Lawson Wilkins and his assistants, and in consultation with my colleagues in psychiatric-endocrine research, Joan G. Hampson and John L. Hampson, Assistant Professors of Psychiatry, The Johns Hopkins University.

* References 1-7.

and to increase this dosage, as speedily as was consistent with medical safety, by increments of ¼ grain (15 mg.) or ½ grain until the optimal therapeutic results were attained or the limits of tolerance had been reached. Most patients under 2 or 3 years of age were found to require 1 to 2 grains (60 to 120 mg.) daily, while those older required 2 to 3 grains (120-195 mg.) daily.

No attempt was made to calculate an I. Q. before children reached the age of 2 years, which is the chronological age when the Revised Stanford-Binet Intelligence Scale can first be used.† It was considered desirable to use as few different intelligence scales as possible, since an I. Q. obtained on one scale is not precisely identical with that obtained on another. The Revised Stanford-Binet Scale was used for children between the ages of 2 and 5 years. The Wechsler Intelligence Scale for Children is not standardized for children younger than 5 years. Except for severely retarded children older than 5 years who could not negotiate even its easiest items, the WISC was used for children between the ages of 5 and 16. Patients of 16 or older were given the Wechsler-Bellevue Intelligence Scale, Form I. The Wechsler scales were given preference over the Stanford-Binet Scale, since they are based on sounder statistical mathematics and permit more accurate comparison of I. Q.'s obtained at different age levels, since they provide a better evaluation of the I. Q. in adulthood, and since they have the great advantage of providing both a verbal and a nonverbal I. Q. as well as a full I. Q.‡

Intelligence Quotient Findings

Several different criteria for subdividing the 70 cases into mutually exclusive groups were given due consideration. Some of the possibilities that promised to shed most light on the intelligence level in hypothyroidism had to be abandoned, owing to gaps in the data on some cases. Thus, only in recent years had radioiodine studies been done routinely; so it was not possible to classify all cases on the basis of the presence or absence of a positive radioiodine uptake by the thyroid gland before treatment was begun. Likewise with studies of protein-bound iodine. For the same reason, the entire 70 cases could not be subdivided unequivocally into those with and those without palpable thyroid tissue before treatment, or subdivided on the basis of the age when clinical manifestations of hypothyroidism became unquestionably evident.

All things considered, it proved feasible to subdivide the 70 cases on the basis of only two criteria. First, those with a history pointing definitely to a diagnosis of co-called acquired hypothyroidism were separated from the congenital cases. Second, the congenital cases were subdivided according to the age at which euthyroidism was established. I. Q. findings are listed in the accompanying Table, according to the subdivisions established.

There are three pertinent observations to be made from the data in the Table. First, established knowledge that I. Q. impairment is not a concomitant of acquired hypothyroidism is confirmed. Second, a low or defective I. Q. is not an inevitable concomitant of congenital hypothyroidism: Especially when treatment is begun very early in infancy and euthyroidism is consistently

† Though Gesell Developmental Quotients can be obtained before the age of 2 years, they should never be used as I. Q. equivalents in the appraisal of hypothyroid children.

‡ It is relevant to note that Wechsler scales are so designed as to provide raw scores and scaled scores on each of 10 subtests, with tables for the conversion of summated scaled scores into a verbal, a nonverbal, and a full I. Q. in relation to chronological age. The Stanford-Binet Scale provides only a raw score, namely, the mental age in months, from which the I. Q. is calculated according to the formula:

$$\frac{MA}{CA} \times 100 = I.\,Q.$$

Under ordinary circumstances, and when the testing procedure has been satisfactory, one expects a subject's I. Q. on the Wechsler scales, though not on the Stanford-Binet,[9] to remain virtually constant as chronological age increases. By contrast, one expects the mental age to increase proportionately with chronological age. Logically, then, a significant increase in a cretin's Wechsler I. Q. signifies genuine improvement in intellectual functioning. An increase in a child's mental age without a corresponding increase in I. Q. signifies only that he has grown older in years and is not intellectually at a standstill. It is usually conceded that annual increments in mental age cease by the middle or late teens, in the same way that annual increments in height age cease after adult maturity is reached.

Intelligence Quotients of Seventy Patients with Hypothyroidism

Congenital Hypothyroidism: Age When Euthyroidism Was Established																									Acquired Hypothyroidism		
By 4 Mo.			4-6 Mo.			6-15 Mo.			15 Mo.-2 Yr.			2-3 Yr.			3-4 Yr.			4-6 Yr.			6-8 Yr.			8 Yr. +					
I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.	I.Q.*	Age Tested Yr.	Mo.
a <28	5	4	a 55	4	3	a<50	3	5	c 43	16	..	b 60	7	7	a<43	4	10	b 47	7	9	b 49	11	4	a<12	20	..	c 36	17	..
a <63	5	5	a 81	2	8	a<67	2	9	b 46	5	7	b 67	11	11	b 48	7	7	b 60	8	2	c 60	20	..	c 59	24	..	a 81	3	0
b 75	5	0	a 86	3	8	b 71	11	6	c 62	20	..	b 74	9	0	c 48	18	..	c 90	20	..	c 64	17	..	c 67	23	..	c 88	18	..
a <80	2	6	a 92	4	1	c 74	15	8	a<72	2	8	b 95	6	5	a 68	3	11	b 91	12	10	b 72	9	5	b 68	14	11	c 92	23	..
b 93	5	11	b 96	8	9	b 79	7	2	a 82	4	7	b 95	8	6	b 79	7	7	b 93	13	8	b 75	8	6	b 75	12	8	c 96	18	..
a 111	3	10	b 97	9	4	b 79	14	6	b 83	8	2	c 113	16	..							b 85	8	3	c 82	15	10	b 97	8	7
a 123	2	7	b 107	9	5	b 80	9	9	b 96	11	4										b 89	11	5				b 108	11	9
						a<88	2	0																			c 116	22	..
						c 99	20	..																			b 122	10	1
						a 122	3	1																			c 122	18	..

* a indicates Revised Stanford-Binet Scale; b, Wechsler Intelligence Scale for Children; c, Wechsler-Bellevue Intelligence Scale, Form I. < means the I.Q was calculated on estimated basal M.A., as patient either failed some of the easiest, i.e., second-year level tests, or became too irritable and uncooperative for a basal M. A. to be established.

maintained, it is possible for a congenital cretin subsequently to obtain an I. Q. rating of "average," or even "superior." Third, a good I. Q. rating is not an invariable sequel of very early diagnosis and treatment, even when euthyroidism is speedily and consistently maintained.

Supplementary Clinical Impressions

Obviously, the age at which euthyroidism is established is not the only variable to be taken into account as a prognosticator of eventual I. Q. level in an infant cretin, even though it may be a significant and important variable. It would be gratifying to be able to report the variables that do determine I. Q. level in congenital hypothyroidism. This gratification must be postponed until full-scale study of hypothyroidism in all its aspects is more advanced than at the present time. Meanwhile, it is possible only to present one's clinical impressions as a rough guide.

First, it is clear from inspection of the Table that I. Q.'s in congenital hypothyroidism do not distribute themselves over the full range of the usual normal curve distribution of I. Q.'s. There are too many low and low-average I. Q.'s and not enough in the higher ranges. It appears, in general, that all the I. Q.'s are somewhat reduced, the high down to average and the average to low. One infers, therefore, that if two children of the same age have hypothyroidism of the same degree of severity, and if both begin substitution therapy at the same time and are consistently kept euthyroid, then the one from a family where high I. Q.'s are common is likely to test with a higher I. Q. than the one from a family where high I. Q.'s are uncommon or absent.

Second, it appears that if two hypothyroid children with an equally severe degree of hypothyroidism begin substitution treatment at the same age, and if one is given a large enough dose of medication to ensure constant euthyroidism, the other being treated suboptimally, then the former will test with a higher I. Q. than the latter.

Third, it appears that if two hypothyroid children begin substitution treatment at the same age, and if one of them began life with minimal, though slowly diminishing, thyroid function, the other having been born with complete athyreosis, then the former has a better I. Q. prognosis than the latter.

Fourth, it appears that if two hypothyroid children whose thyroid failure was insidious in onset (goitrous cretins, for example) begin substitution treatment at the same age, then the one who has had a totally nonfunctional thyroid gland for a shorter time will have less I. Q. impairment than the other.

In all varieties of hypothyroidism, the date when thyroid function totally fails, together with the duration of total thyroid failure, appears to be a most important variable in relation to I. Q. impairment. In the Table there are several entries of an I. Q. that is not grossly impaired, despite the fact that treatment was not begun and euthyroidism was not established at an early age. In some of these cases there are enough recorded laboratory and clinical data to furnish substantial evidence that thyroid function, though severely diminished, did not fail completely until after early infancy.

In differentiating complete from partial thyroid failure, tests for radioiodine uptake and for protein-bound iodine or butanol-extractable iodine are instructive. Nonetheless, these tests do not retroactively date the cessation of thyroid function that gradually failed. They cannot, therefore, be expected to yield data that correlate perfectly with I. Q. prognosis in all cases.

The problem of the relationship between I. Q. impairment and the age at which thyroid failure became complete is all the more baffling as very little is known about thyroid function, or its failure, in the fetus. A great deal needs to be ascertained, for instance, about transmission of thyroid hormones across the placenta and the role of maternal hormone in adequately protecting a thyroid-defective baby.[10] New research on cyanocobalamin (vitamin B_{12}) levels in

hypothyroidism is worth keeping an eye on, in connection with thyroid deficiency in the newborn.[11] In the meantime, one may very legitimately conjecture that the fetal age of onset of thyroid failure has an important bearing on the severity and permanence with which the central nervous system, and eventually its functioning during a test for I. Q., is adversely affected. It seems highly likely that the fetal and early postnatal months of neural differentiation and myelination are crucial months so far as the permanent mental sequelae of thyroid deficiency are concerned.

Histopathological evidence of structural anomalies in the development of the central nervous system in hypothyroidism has not been assiduously sought for. The investigation recently reported by Horn[12] is, therefore, especially valuable. Horn studied, among other things, the effects of I^{131}-induced athyreosis on the cerebral development of rats from birth to 60 days. He found that the total number of nerve cell bodies in the striate area of the cerebral cortex was constant in all the animals, experimental and control, whereas the density of the fiber network was significantly low in the untreated athyreotic animals. These animals had small brains with closely packed cells of reduced size, the high cell concentration being associated with a low fiber density. Such anomalous brain development was not observed in athyreotic animals left untreated for the first 24 days of life and subsequently given thyroid substitution therapy. Horn's experiment was not designed to provide any data on the duration of athyreosis in relation to irreversibility of defective cerebral development.

Central Nervous System Impairment

There are many and varied signs of impaired neural functioning in human beings with hypothyroidism. An unmistakable sign is the lethargic inertia so characteristic of untreated hypothyroid patients. Admittedly, this inertia cannot be attributed exclusively to sluggish transmission of messages within the central nervous system. Nonetheless, specific impairment of neural function can be measured as a gross inability to form conditioned reflexes.[13] When a hypothyroid patient is tested before and after thyroid substitution therapy, there is, within the first month of treatment, a dramatic increase in the speed with which conditioned reflexes can be established. Further evidence of impaired neural function in hypothyroidism is provided by the frequent finding of marked slowing in the EEG record—a finding which soon disappears after thyroid therapy is instituted.§

Still further evidence of impaired neural functioning can be obtained from hypothyroid patients under treatment. After euthyroidism has been established, some congenital cretins manifest chronic signs of neurological impairment. These signs include hyperactive deep tendon reflexes, spasticity of the limbs, clumsy awkwardness, and muscular incoordination, with trembling and jerkiness when precision movements are attempted. In the present sample of 60 congenital cases, 4 patients showed gross signs of spasticity and 6 others had noticeably awkward, unsteady muscular coordination. All 10 tested with an I. Q. below 65. The two lowest I. Q.'s in the entire series were <12 and <28, and in each instance the patient was severely spastic and unable to walk properly. Though the young woman with I. Q. <12 was still hypothyroid after the age of 8 years, the 5-year-old child with I. Q. <28 was euthyroid by the age of 4 months. It appears likely that severe neurological impairment is not reversible by early thyroid therapy. Exactly how well severe neurological impairment correlates with severe I. Q. impairment cannot be precisely determined from the data of the present study. The data do strongly suggest, however, that the worse the signs of neurological impairment, the worse the prognosis for the I. Q.

§ Ross and Schwab.[14] Marshall, C., and Pearson, P. H.: Data to be published from the electroencephalographic laboratory, The Johns Hopkins Hospital.

Communicational Signs of Impaired Neural Functioning

Except in a few instances of early diagnosis and treatment with thyroid, speech development is much delayed in infants with a history of hypothyroidism. Excessive delay of speech development in these infants may be an indicator of gross and permanent I. Q. impairment, though by no means inevitably so. Among young hypothyroid children on substitution therapy, there are many so slow in speech development that they cannot negotiate the verbal items at the second-year level of an intelligence test when they reach the chronological age of 3, or even 4, years. These children, therefore, obtain a rating on the test at the "mentally defective" level. Two or three years later, however, after the onset of verbal communication, these same children may retest with a rating of "dull-normal" and occasionally as high as "average."

When their speech development has been much delayed, many hypothyroid children subsequently pass through a stage, sometimes prolonged, of having great difficulty with the vocal mechanics of speech. They are slow in advancing beyond the stage of baby talk in which consonants are incorrectly articulated or omitted. The phonic distortions that result may be so idiosyncratic that only the mother, through her close contact with the child, is able to decipher their meaning. Some of these children also go through a protracted period of being almost totally inhibited in speech whenever their inability to conform to the simple orthodoxies of speech will become conspicuous. Thus, they will negotiate the nonverbal, but not the verbal, items of an intelligence scale. In some cases speech inhibition is only partial, so that the child makes a few responses, though only in an unvocalized whisper. On such occasions parents are usually dismayed, for they report that their child usually talks quite freely at home. Such children talk with their greatest fluency when they are not prompted to talk about a preordained topic or questioned for specific information. It is prompting and questioning that promote inhibition of their poorly stabilized mastery of vocal neuromuscular coordination.

Tested at a time when speech development is still greatly in arrears, hypothyroid children achieve a low I. Q. insofar as they cannot negotiate verbal subtests. As speech development advances, some of these children retest with a higher, though not necessarily a good, I. Q. Even if the I. Q. stabilizes below the dull-normal level, chronic residual speech impairment is by no means inevitable. In other words, further improvement in enunciation and articulation is possible after the I. Q. has stabilized. Chronic speech defect is not, however, exclusively concomitant with the lowest grades of I. Q., though it appears exceptional for a persistent speech defect to be associated with an I. Q. of average or higher.

In the present sample of 60 patients with congenital hypothyroidism there were, among those over the age of 8 years, 10 who had a persisting speech defect of one sort or another. The highest I. Q. in this group was 91; the other I. Q.'s ranged from 83 to <12. The 12-year-old boy with an I. Q. of 91 had a highly specific and peculiar inability to enunciate unfamiliar polysyllabic words, like "archeologist," after as many as 20 trials. He would have to start saying the word from the beginning many times, because the middle syllables jumbled with one another, though he was able to enunciate each syllable as an isolated unit. The young woman with an I. Q. of <12 showed the grossest kind of arrestment at a stage of infantile articulation. Four other patients evidenced persistence of infantile articulation, notably omission, elision, and substitution of consonants. In two patients the speech difficulty was true stuttering. Finally, two patients were severely affected with multiple speech anomalies involving dyscoordination of respiratory and facial muscles used in speech, repetitions and omissions of words or phrases, and true stuttering. These two severest cases of

speech disorder were also cases of very low I. Q., namely, 59 and 67.

Difficulties with the mechanics of speech constitute one group of communicational signs of impaired neural functioning. Another such group of signs pertains more specifically to difficulties in the realm of language, thought, and meaning. These difficulties may be summed up under the name dysgestaltism, that is, an impairment of ability to form cohesive cognitional patterns, configurations, or Gestalten. Impaired Gestalt formation may or may not be accompanied by impedances in the vocal mechanics of speech production. It may be mild and outgrown after early childhood, or severer and long-lasting.

Signs of Gestalt impairment often do not appear in the course of casual conversation, such as takes place during a physical examination. They come to the fore most conspicuously when a patient does not set the tenor and topics of conversation himself, but when he is requested to comply with specific instructions for which a right or a wrong response is possible. Thus an intelligence test provides an excellent setting in which to elicit signs of Gestalt impairment.

Signs of Gestalt impairment appear when a person might have said "I don't know," or "I can't do it." Instead, he makes an attempt at the problem and produces a response earmarked in one of several characteristic ways. One of the most telltale of these earmarks is perseveration; that is, the response is a repetition or carry-over of a response to a previous question, despite its irrelevance to the question in hand. The person has been unable to make a switch from one question to the next.

EXAMPLE 1.—"Nonsense" and "hero" are two consecutive words on the vocabulary subtest of the Wechsler children's scale. A 12-year-old girl, I. Q. 67, defined them as follows: "You're nonsense when you don't do it." Then, "You're a hero when you do something right. If you're playing soldiers and you ask a silly question and the man tells you nonsense, it means you don't know what you're saying." From what she said, it is evident that the girl had a workable conception of the meaning of each word, but the Gestalt or pattern for defining this meaning was jumbled and the definition of the first word perseverated into the definition of the second.

EXAMPLE 2.—The questions and answers on three successive items in the information subtest of the Weschler children's scale are recorded as follows for a girl of 7 years, 7 months, I. Q. 60:

From what animal do we get milk?	White milk. I get white. My dog's milk.
What must you do to make water boil?	I make it for the dog. The dog drinks milk and I drink chocolate milk.
In what kind of store do we buy sugar?	I buy it for my dog. I get it for the dog, for a meal.

Perseverative carry-over from one question to the next makes the foregoing answers strictly irrelevant, though the perseveration is not verbatim repetition. In extreme instances, perseveration can manifest itself as verbatim reiteration of a word or phrase in response to successive questions.

Another earmark of impaired Gestalt formation is an inability, resembling aphasia or paraphasia, to find the precise word or phrase that carries the meaning of what one tries to say.

EXAMPLE 3.—The first two items of the Wechsler Picture Completion subtest are a comb with a tooth missing and a table with a leg missing. The responses of an 8-year-old girl, I. Q. 83, were perserverative, as well as aphasic. For the first her response was: "Two of these sticks"; for the second: "A stick from a table, for a table."

EXAMPLE 4.—The word thermometer was defined as follows by a man of 23, I. Q. 67. "A thermometer has got something to do with the weather. I know it's marked in degrees, but that's all I can say about it."

EXAMPLE 5.—Slowly and with an expression of intense struggle, a young woman of 18 with I. Q. of 48 finally defined a letter as "Paper." Pressed for more information, she added: "It's an envelope." She was shown a small scrap of paper and asked if it were a letter. "No," she said, "it's big." To a request to tell something further about a letter, she replied: "And on top of it is a er——" and then, after a long pause, with her lips moving as if looking for a word, " . . . flowers." When asked if a letter had writing on it, she said "Yes," with obvious pleasure.

EXAMPLE 6.—A woman of 24, with I. Q. 59, whose speech was severely impeded by stuttering and repetitiousness, defined a nail thus: "The nail, the nail, is the er, of er, is the er, silver things, and you do a lot with it." "Tell me what you do," the examiner asked. "You can make them of er, chairs, wagons, bikes, toys; hang up the curtain, fix up something with it, and to make the desk and houses, and lots of things."

The foregoing examples represent auditory-vocal aphasic tendencies. Visual and motor aphasic tendencies were identified less frequently, perhaps because of the preponderant emphasis on speaking in an intelligence test.

EXAMPLE 7.—The same boy, age 12 years 10 months, I. Q. 91, who had great difficulty in articulating polysyllabic words, also had a severe reading disability. He had difficulty in recognizing printed words, sometimes recognizing familiar words, sometimes not. In writing, he made frequent reversals, for example, *b* for *d*. He also reversed the direction of some lines and curves while copying figures of the Bender visual-motor Gestalt designs. He omitted letters when copying sentences and transcribed wrong letters when a word was spelled out for him—"squarn" for "square" and, upon repetition, "squaen." In addition, the boy was left-handed.

Among the group of 60 patients, the signs of impaired Gestalt formation were seldom perseverative or aphasic alone. Commonly they were accompanied by periphrasis, a long-winded sequence of peripherally related ideas and associations. Sometimes periphrasis betrayed not only perseveration and an aphasic search for words but also an inability to screen out and reject various tangential associations. Such tangential associations sometimes bore identifiable relevance to the examiner's inquiry, but in some instances the logic holding them together was concealed and needed additional information for its decipherment.

EXAMPLE 8.—The abstract idea of similarity baffled the man who had trouble in defining the word thermometer. For the similarity between a coat and a dress, he said: "A coat is something you slip over, and a dress buttons up." Inquiry was pursued, and he added: "I know you don't put your coat tail in your pants. I just know there is a difference in some way."

EXAMPLE 9.—"You wear," responded a boy of 9 years 8 months, and an I. Q. of 74, for his definition of the word hat. He added, upon prompting: "And clothes you wear. Keeps you warm. If you didn't wear a hat you could catch a cold or a disease, all sorts of diseases." The next vocabulary word was letter. He replied: "You take a piece of paper and write, 'What are you doing and how do you feel?' It means you feel fine—so many things I can't name them. And a coat keeps you warm, and you don't get diseases. The same thing I just told you about other things. And (looking at an examining table) a bed you rest in and sleep on all the night. And I forget the rest. And a typewriter you write on, or you could make a newspaper."

EXAMPLE 10.—On the similarities subtest, a boy of 6 years 5 months and an I. Q. of 95 said of beer and wine: "They are bitter." Then he talked at considerable length about a watch his uncle had given him. Urged for more information on the similarity of beer and wine, he replied: "They're the same, but I don't know how." Urged further, he said: "Well, an apple (the previous question had been about a plum and a peach, to which he had associated apple) is different from wine or whisky, and an apple or a red tomato." Working on a hunch, the examiner checked with the boy's parents and ascertained that the boy was first introduced to a taste of wine of the red variety at a party on which occasion his uncle gave him a watch. Thus, there is a hidden chain of logic in the hodgepodge of the boy's answers.

Impairment of Gestalt formation may be disclosed in yet a fourth way, namely, by changing the subject. In its crassest form, changing the subject appears to be a random naming of nearby objects and sounds or a demonstration of elementary skills, as though the subject wanted to please the examiner by displaying his attainments to compensate for his failure on test assignments.

EXAMPLE 11.—The patient with I. Q. <12 was a young woman of 20. The first item on her vocabulary subtest was the word apple. Her response was: "Boy." Further requests for more information led to the following replies: "Raining?" (She had heard a noise like rain and pointed outside. She had asked this question several times before, and asked it again several times subsequently.) "Table." "Boo! Ah-boo! and Boooo!" (exclaiming like a very young infant). "There you are." Another of her verbal accomplishments, often repeated, was to call: "Audrey!," like a mother calling a child from play.

Changing the subject may also be done with more meaningfully organized sentences, in the manner of a digression.

EXAMPLE 12.—A youth of 16, who tested with an I. Q. of 43, habitually, in and out of the testing session, had something to tell the examiner. He did so characteristically with a husky whisper, as though in great confidence. A typical example came as a sequel to the question, 'Why are shoes made of leather?' "I don't know, just to wear them. Next week I get a license. I have to be able to drive a car. When I get big I have to have a car—when I get big and work."

Whereas some children would divert with a change of subject, others, especially the younger ones, would burst into an unexpected torrent of tears, and thus find respite from a task that had become too grueling and catastrophic. The contrary reaction in young children was an exaggerated outburst of joy whenever a difficult operation, requiring sustained concentration and effort, terminated in success.

In 22 of the 60 congenital cases, one or more of the foregoing signs of impaired Gestalt formation was noted. One should not attribute too much importance to this figure, however, for it does not take account of Gestalt impairment in the younger children at the preschool level of development. These children were communicationally too immature for the above types of sign to appear during a testing session. In them the signs of Gestalt impairment were different. Perseveration, insofar as it did appear, showed itself as inability to cease playing with one group of test materials and shift attention to another test assignment. When the children were taxed to the utmost of their ability, commonly they became either silent and immobile or antagonistically rebellious, signaling the examiner away and thrusting test materials away. It was conspicuous that signs of stubbornness and negativism largely disappeared after a child had advanced developmentally to a stage of being able to say that something was too hard for him, or that he didn't know the answer. Ability to state and use these two propositions emerged much later, on the whole, than in ordinary children, dependent on the degree of cognitional impairment involved.

Contrariness in Hypothyroid Patients

Inertia, indifference, stubbornness, and antagonism are common personality characteristics in children with a history of congenital or acquired hypothyroidism. These personality characteristics are, in all likelihood, intimately associated with the natural history of thyroid deficiency and its correction.

Initially, hypothyroid infants are lethargic and inert, so much so in severe cases that one interprets their inertia and indifference as such and seldom makes the misinterpretation of stubbornness or antagonism. The earlier these infants are diagnosed and brought to euthyroidism, the greater are the chances that their over-all psychologic development will parallel that of the ordinary child. The longer their diagnosis and treatment is delayed, the longer will they remain lethargic and inert, all of their developmental functions inhibited. In general rearing and management, they will be untroublesome — too untroublesome — in the sense that they display no active striving toward mastery and accomplishment. It is only as their lack of mastery shows up irrefutably as retardation that parents become troubled and recognize that a problem exists.

It is not uncommon that hypothyroidism has remained undiagnosed until the age of 3 or 4 years, or even longer. When, at such an age, a child is first put on thyroid medication, he very suddenly undergoes a dramatic release of energy and animation. Unlike other children of his own age, he has had no slowly acquired experience of applying regulatory controls to this new resource of vigor. He has not worked out a nice balance between assertion and compliance. One of the first things likely to happen is that the wild horses of his new vigor bolt and run wild. The child becomes an assertive being in his own right for the first time. A very effective technique of

self-assertion is to refuse and say "no." Newly treated hypothyroid children often go on a spree of refusing and rebelling. So rapid is the transition from compliant inertia, and so exaggerated is self-assertiveness, that many of these children are, for a time, very trying to live with.

The phenomenon of a spree of refusing and rebelling is not limited to congenital cretins under treatment. It is also encountered in children whose hypothyroidism indisputably had its onset long after birth. These children have no concomitant I. Q. impairment. Their negativism is not, therefore, in any way connected with I. Q. impairment. In children whose hypothyroidism dated from birth, and whose I. Q. is impaired, one may also encounter negativism. In addition, however, one encounters simple indifference, immobility, or silence when the child is unable to understand a request and respond as expected. Such nonparticipation has the surface appearance of stubborn obstinacy and negativism—indeed, it may change to a fit of crying or of temper. It is difficult, sometimes impossible, to distinguish this kind of indifferent nonparticipation from defiant stubbornness and refusal to perform some familiar, well-practiced operation.

Refusal, obstinacy, rebellion—they all need shrewd handling on the part of parents, for they are the stuff of which autonomy, independence, and initiative are made. Wise parents do not tolerate contrariness in undiluted quantities, though they certainly do not squelch it with dictatorial intolerance. The parent of a hypothyroid child recently begun on thyroid therapy has a special job to do in assisting the child competently to impose a system of checks and balances on the vigor and animation that thyroid releases. This special job may last for two or three years. Some children appear to have much more of a task on their hand than do others, in this respect. In fact, there are a few children who, when judged euthyroid by the usual clinical and laboratory criteria, resemble hyperthyroid children in their hyperkinetic behavior and flighty attention span. At the opposite extreme, there are patients who, though judged euthyroid, are exceptionally slow in their movements, lassitudinous, and generally lacking in vigor and alertness. Perhaps they are the counterpart of so-called apathetic hyperthyroidism. These extremes so far as behavioral and psychologic signs are concerned suggest the hypothesis that central nervous system functioning does not always have the same threshold of sensitivity to desiccated thyroid, or maybe to one of its component hormones, as do other bodily functions.

Only on a basis of sound clinical judgment, different for each subject, can one decide how to regulate thyroid dosage in extreme cases of hyperactivity or lassitude when the patient otherwise appears euthyroid. On the basis of present evidence, mental development is too greatly imperiled to justify lowering of an optimal thyroid dosage in order to control hyperactivity and irritability in young infants. In older children, it may be wise not to lower the dosage of thyroid permanently, but to postpone the period of their becoming adapted to an optimal thyroid dosage until, say, the long school vacation, when everyone concerned may be better able to cope with the behavioral disruptions of the period of adaptation. In some instances, it may prove good clinical judgment to maintain an older, especially a nonjuvenile patient, at a level of slight hypothyroidism, but this practice should not be espoused as the treatment of choice. Patients who, though judged euthyroid, are lassitudinous do not commonly become more vigorous on an increased dosage of desiccated thyroid. Recent work on the therapeutic use of *l*-thyroxine and *l*-triiodothyronine instead of desiccated thyroid for nonmyxedematous patients with hypometabolism and lassitude [15] is worthy of further evaluation in this respect.

I. Q. Constancy

Nonparticipative contrariness in older untreated cretins and more overt contrariness

in those recently made euthyroid greatly restrict the degree of cooperation with which these children can negotiate an intelligence test. Often one is justified in reporting only that the result was inconclusive, or that the child was still at the level of pretest mentality. Nonetheless, since contrariness is so intimately connected with congenital deficiency and intellectual impairment, one is also justified in estimating an I. Q. figure as accurately as possible, prorating from the child's incomplete performance. This estimate is justified insofar as it gives a figure against which to compare future I. Q. figures. The estimate is justified, however, only if one scrupulously avoids the error of considering that the I. Q. obtained in the early stages of a cretin's therapeutic career is inevitably fixed and permanent.

So far as the evidence goes, there are some hypothyroid children whose I. Q. has not changed significantly after the first time they were tested. There are others, by contrast, who have remained at a level of pretest mentality for some months after thyroid treatment was instituted, then have obtained a low I. Q. for one or two years, and finally have tested at higher level.

EXAMPLE 13.—A girl whose hypothyroidism was of the goitrous type and had been of slow, insidious onset, was first diagnosed at the age of 6 years 2 months. At that time, before thyroid treatment was begun, she did none of the verbal subtests on the Wechsler children's scale. On the nonverbal scale she obtained an estimated I. Q. of 79. At the age of 6 years 5 months, after three months on treatment, the same test was repeated, with these results: verbal I. Q. 56; nonverbal I. Q. 74; full I. Q. 61. She was maintained consistently at the euthyroid level, and the test was twice readministered. At 7 years 3 months of age, the verbal I. Q. was 80, the nonverbal I. Q. 71, the full I. Q. 73. At 9 years 5 months of age, the verbal I. Q. was 70, the nonverbal I. Q. 80, the full I. Q. 72.

EXAMPLE 14.—Another patient, a boy, also had hypothyroidism of the goitrous type and of insidious onset. At the age of 11 months thyroid therapy was begun, but the dosage was small and inadequate. At the age of 2 years 11 months he was for the first time given enough medication to produce euthyroidism. At that time he was so retarded at the level of pretest mentality that an I. Q. could not be even tentatively estimated. At the age of 4 years 6 months the Revised Stanford-Binet Scale was administered in a hotel room, since the child was panicky and in turmoil every time he entered the hospital. The I. Q. obtained was 89. When the boy was 6 years 5 months old, his result on the Wechsler children's scale was as follows: verbal I. Q. 109; nonverbal I. Q. 80; full I. Q. 95.

EXAMPLE 15.—Gross hypothyroidism of acute onset was diagnosed in a boy of 2 months, and effective therapy was instituted forthwith. At the age of 2 years 2 months his I. Q. on the Revised Stanford-Binet Scale was 100. On the same scale, at the age of 4 years 3 months, his I. Q. was 111.

EXAMPLE 16.—A girl with cretinism of the severest, textbook variety was brought in for diagnosis at the age of 4 years 2 months. At that time she was totally incapable of making any response of the type required on an intelligence test. At the age of 6 years 0 months she obtained an I. Q. of 51 on the Revised Stanford-Binet Scale. Eleven months later, the girl literally and precisely did what her parents had prepared her for; namely, she played with the test toys and steadfastly would have nothing to do with test questions and instructions. At 7 years 9 months, on the Wechsler children's scale her ratings were as follows: verbal I. Q. 56; nonverbal I. Q. 47, full I. Q. 47.

The entire issue of constancy of the I. Q. in hypothyroidism is gravely complicated by the not well-known fact that the Revised Stanford-Binet Scale does not yield a constant I. Q., as chronological age increases, especially in cases of low or high I. Q.[9] Thus, on this scale, a child who achieved an I. Q. of 75 at 6 years of age would, despite continued mental growth commensurate with his level of intellectual ability, obtain an I. Q. of 60 at the age of 12 years. The Wechsler scales are so constructed as to eliminate this defect, but they cannot be used below the age of 5 years. The present study does not include enough instances of children repeatedly tested with Wechsler scales to permit a definitive statement about I. Q. constancy or inconstancy.

Once, again, one must rely on clinical impression, on which basis it appears that it is unsafe to expect a hypothyroid child's I. Q. to be constant within the first two years after euthyroidism is established. It may take as long as five years before the

child's I. Q. stabilizes, subsequent retestings thenceforth giving a virtually constant figure. Instances in which the I. Q. increases after five years of euthyroidism are apparently exceptionally rare.

To say the same thing in another way: It appears that it may take as long as five years before a child with a history of hypothyroidism recovers mentally from the abnormal growth patterns induced by hypothyroidism. Thereafter mental growth probably follows the pattern of the usual growth curve for mental functioning, which, incidentally, is an asymmetrical curve, and not simply a sloping straight line.[9] As in the case of stature, annual increments of mental growth are not equal in amount.

Psychologic Recommendations for Case Management

1. Beyond all possible shadow of doubt, the most important single step in the psychologic management of hypothyroidism is to prevent, as much as possible, the disabling sequelae of thyroid deficiency by making a prompt diagnosis and thenceforth consistently maintaining the patient at the level of euthyroidism. Whenever there is the slightest suspicion of hypothyroidism, especially in a young infant, the case should be immediately referred for definitive laboratory tests and expert clinical evaluation. In the early weeks and months of life, every day is prognostically of immense value, and there should be no procrastination in correcting hypothyroidism to euthyroidism.

2. Whether a hypothyroid child has a low, average, or high I. Q., and whether the condition is congenital or acquired, the parents are helped to do a better job of rearing if they have an opportunity, from time to time, to discuss the commonness, significance, and management of contrariness in children with a hypothyroid history. They are especially helped to know that, when wisely and shrewdly handled, contrariness does not ordinarily remain a permanent feature of the personality of children with a history of hypothyroidism. The parents of hypothyroid children also find it helpful to know in advance that they may expect the advent of contrariness, in one guise of another, dependent on the child's age, after substitution therapy is commenced, and to know that they may have to prepare themselves to be patient, comprehending, and tolerant in the trying period ahead. Otherwise, they may attribute naughtiness and willful disobedience to the child and, by being too disciplinary or too indulgent, contribute to a vicious circle of psychologic nonhealthiness.

3. There is still, in the present day, sufficient social stigma attached to terms like "mentally defective" and "retarded" that some parents fail to assimilate and to act upon the knowledge that their congenitally hypothyroid child has a severe mental handicap, if such terms are used in explanations given by a specialist. Parents comprehend much better the difficulties their child has if they are explained in terms of an analogy between the human brain and a central telephone office in a large city—an analogy that refers to messages and their blockage, the use of auxiliary roundabout routes, and so forth. This analogy makes a lot of sense to these parents, for it puts into words their own observations of their child, whose mental impairment is often patchy, so that he does one thing fairly well but not another, or succeeds with a task one day and fails it the next.

4. Once they have assimilated the idea that their child has a severe mental handicap, some parents still fail to assimilate the idea that the child will require special education. Again it is social stigma attached to terms like "schools for backward children" that stalls them. They are helped, therefore, by an explanation that special classes are special because they provide superior opportunities for individual instruction which their child with a learning handicap will need. These parents are also helped by explicit advice concerning the practicalities of getting their child enrolled in a special class. The great majority of children with

a history of treated congenital hypothyroidism have proved educable if such special provisions are made and do not require permanent custodial care in an institution. Even in those cases where the I. Q. is as high as the borderline or dull-normal level, the child usually benefits a great deal from being educated in a special class instead of the crowded classroom of an ordinary grade school.

5. It is wise, when a child with a history of hypothyroidism gets old enough to be able to understand the explanation, to tell him in elementary outline the nature of his condition and why he will need to keep taking thyroid medication throughout life. A few patients evolve personal theories that they are chronic invalids and victims of thyroid disease. A few parents entertain similar ideas about their child, even when the I. Q. is not severely impaired. These ideas can usually be corrected if thyroid pills are likened not to medicine but to a special food which needs to be taken in concentrated form by people with underactive thyroid glands.

6. Older girls with a history of hypothyroidism should be warned to consult an endocrinologist should they become pregnant, so that their thyroid status can be regulated throughout the pregnancy.

Summary

With due regard for unbiased statistical sampling, 70 children and young adults with a history of hypothyroidism were tested for their I. Q. Established knowledge that I. Q. impairment is not a concomitant of acquired hypothyroidism was confirmed. It was also found that a low or defective I. Q. is not an inevitable concomitant of congenital hypothyroidism. Especially when treatment is begun very early in infancy and euthyroidism is consistently maintained, it is possible for a congenital cretin subsequently to obtain an I. Q. rating of "average," or even "superior." Nonetheless, a good I. Q. rating is not an invariable sequel of very early diagnosis, even when euthyroidism is speedily and consistently maintained. On the basis of supplementary clinical impressions, it appears that not one but several variables need to be considered in relation to the ultimate prognosis of I. Q. in children with a history of hypothyroidism. The variables include familial frequency of high, average, and low I. Q.'s; age, including fetal age, when thyroid function failed; duration of complete athyreosis; adequacy of dosage once substitution therapy is begun and the constancy with which euthyroidism is maintained, and the time interval between establishment of euthyroidism and evaluation of I. Q. I. Q. impairment in hypothyroidism is associated with impairment of Gestalt formation, cognitionally, and thus of impairment of the human communicational function in general. The vocal mechanics of communication are also likely to be impaired. In severe cases, classical signs of neurological impairment may also be encountered. Contrariness in various guises is a common, though not irreversible, personality trait in children with a hypothyroid history. This contrariness has bearings on I. Q. constancy, as the I. Q. often does not stabilize until between 2 and 5 years after euthyroidism is established, during which period contrariness is most in evidence. Psychologic recommendations for case management pertain, in brief, to the primary importance of prompt and optimal thyroid substitution therapy and to the advice and guidance that is beneficial to parents and patients alike.

REFERENCES

1. Brown, A. W.; Bronstein, I. P., and Kraines, R.: Hypothyroidism and Cretinism in Childhood: VI. Influence of Thyroid Therapy on Mental Growth, Am. J. Dis. Child. 57:517, 1939.

2. Goodkind, R. P., and Higgins, H. L.: Hypothyroidism in Infants and Children with Reference to the Ultimate Prognosis Concerning Intelligence and to the Withdrawal of Thyroid Therapy as a Diagnostic Measure, New England J. Med. 224:722, 1941.

3. Bruch, H., and McCune, D. J.: Mental Development of Congenitally Hypothyroid Children: Its Relationship to Physical Development

and Adequacy of Treatment, Am. J. Dis. Child. 67:205, 1944.

4. Radwin, L. S.: Michelson, J. P.; Berman, A. B., and Kramer, B.: End-Results in Treatment of Congenital Hypothyroidism, Am. J. Dis. Child. 78:821, 1949.

5. Topper, A.: Mental Achievement of Congenitally Hypothyroid Children: A Follow-up Study of 20 Cases, A. M. A. Am. J. Dis. Child. 81:233, 1951.

6. Lawson, D.: On the Prognosis of Cretinism, Arch. Dis. Childhood, 30:75, 1955.

7. Smith, D. W.; Blizzard, R. M., and Wilkins, L.: Mental Attainments of 128 Hypothyroid Children According to the Type of Disease and Time of Treatment, Pediatrics, to be published.

8. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield, Ill., Charles C Thomas, Publisher, 1950; See also revised second edition, to be published.

9. Wechsler, D.: The Measurement of Adult Intelligence, Ed. 3, Baltimore, The Williams & Wilkins Company, 1944, Chap. 3.

10. Peterson, R. R., and Young, W. C.: The Problem of Placental Permeability for Thyrotrophin, Propylthiouracil and Thyroxine in the Guinea Pig, Endocrinology 50:218, 1952.

11. Okuda, K.; Hellegers, A. E., and Chow, B. F.: Vitamin B_{12} Serum Level and Pregnancy, J. Clin. Endocrinol., to be published.

12. Horn, G.: Thyroid Deficiency and Inanition: The Effects of Replacement Therapy on the Development of the Cerebral Cortex of Young Albino Rats, Anat. Rec. 121:63, 1955.

13. Gantt, W. H., and Fleischmann, W.: Effect of Thyroid Therapy on the Conditional Reflex Function in Hypothyroidism, Am. J. Psychiat. 104:673, 1948.

14. Ross, D. A., and Schwab, R. S.: The Cortical Alpha Rhythm in Thyroid Disorders, Endocrinology 25:75, 1939.

15. Kurland, G. S.; Hamolsky, M. W., and Freedberg, A. S.: Studies in Non-Myxedematous Hypometabolism: The Clinical Syndrome and the Effects of Triiodothyronine, Alone or Combined with Thyroxine, J. Clin. Endocrinol. 15:1354, 1955.

Clinical Relationship of Enuresis to Sleepwalking and Epilepsy

Lt. CHESTER M. PIERCE (MC), U.S.N.R.
and
Capt. HARRY H. LIPCON (MC), U.S.N.

Early in the course of a research study designed to elucidate further channels for investigating symptomatic immaturity habits (enuresis, sleepwalking, stuttering) in servicemen, it was decided to seek clinical correlations of enuresis, sleepwalking, and epilepsy.* This decision was subsequent to the discovery that adolescent male enuretics and adolescent male sleepwalkers had significantly more electroencephalographic abnormality than a control group. In addition, members of both experimental groups gave histories which either had been confirmed for or were suggestive of epilepsy. The finding that the sleepwalkers commonly (61.8%) had had a problem of enuresis, and that many enuretics (26.6%) were sleepwalkers, therefore directed an inquiry into the statistical relationships of enuresis, somnambulism, and epilepsy.

After interviews with an additional 200 enuretics and an additional 200 nonenuretics, it was concluded that the enuretic is more likely to have a family history of enuresis, epilepsy, and sleepwalking, a past history of somnambulism, and a past history of epilepsy. The purpose of this report is to call attention to these relationships in the hope that if they are verified they will be of ultimate value in the formulation of neurophysiologic concepts.

Received for publication April 27, 1956.

The opinions or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

* References 1-4.

Definitions

In this study Wilson's definition of enuresis was employed.[5] "Enuresis, then, can be defined as bed- or clothes-wetting [in those] above the age of three, who fail to inhibit the reflex when the impulse is felt during waking hours, or do not rouse from sleep of their own accord when the process is imminent."

The family history was obtained after each man had been told that "family" included brothers, sisters, parents, grandparents, aunts, uncles, first cousins, nephews, and nieces. All 400 interviews were conducted by the same examiner (C.M.P.), who took care to assure that only blood relatives were included in the tabulations.

Method and Material

Two hundred enuretic Naval recruits who were discharged from the service at the U. S. Naval Training Center, Great Lakes, Ill., and 200 nonenuretic Naval recruits who had only one week left to complete training were interviewed in regard to (1) past history of enuresis, sleepwalking, and epilepsy; (2) family history of enuresis, sleepwalking, and epilepsy, and (3) history of faulty dentition.

Many youths who are unmotivated for further service will resort to deliberate bedwetting in order to effect a discharge from the Navy. To guard against including such persons in this study, all enuretics had to meet rigid qualifications. On all 200 subjects a report from a social service agency in their home town had to indicate a lifelong problem with enuresis. These reports always contained a verification from family members and often statements from school authorities or family doctors. Secondly, the subject had to have noted on a document he filled out upon entrance to the service that he had some problem with bedwetting after age nine. Thirdly, all subjects had to admit in interview that they had bed-wet while in the service. In addition to the social service verification, admitted past history, and documentation of past history, most of the recruits had been observed to be enuretic by their company commanders and by trained hospital corpsmen.

Both the epileptologist and the dentist have long been concerned with calcium metabolism and the

function of cholinesterase and its relationship to acetylcholine and potassium.† The common research interest was called to mind after observation of nearly 23,000 recruits indicated that enuretics might have more dental trouble than nonenuretics.‡ This knowledge plus reports of the experimental production of gingivitis [13] and bladder disturbances [14] via central nervous system lesions led to a consideration of dental health in the enuretic.

A gross index to adequacy of dentition is provided by determining which recruits were able to enter training immediately, without being detained for corrective oral treatment, in a "Dental Holding" company. The recruit placed in "Dental Holding" is in the custody of the dentists, before he is allowed to enter formal training. Accordingly, a history of placement in "Dental Holding" was included in this investigation.

The controls were men from regular training companies which had almost completed recruit training. This means that none had been discovered to be enuretic while in training, since such a discovery eventuates in quick separation from the service. The chosen companies were selected at random by a line officer. The members of the company were interviewed individually, though they arrived for the interview in masses, along with their peers.

In the procurement of data such variables as age, geographic influence, diet, and sociocultural conditions are not thought to have limited the study as much as the traditional obstacles of ignorance and concealment of material by the informants. Roughly, all the recruits studied were teen-age youths from middle-western and southern states who usually belonged to the lower or lower-middle class.

Results

In this study the enuretic is over seven times as likely as the control to have a family history of enuresis and over four times as likely to have a family history of somnambulism. The enuretic group contains over three times as many men who can tell of a past history of sleepwalking. There is also a definite trend toward a statistically pertinent past history of epilepsy among the enuretics. It is found that upon entrance into the service over one and one-half times as many enuretics as controls were in need of dental care prior to admission to recruit training. Table 1 summarizes the interview results.

Twelve controls (6%) admitted a problem of enuresis at ages ranging between 9 and 18 years. Of these 12 subjects, 5 (2.5%) had no other positive findings in regard to a family history of enuresis, sleepwalking, or epilepsy or a past history

TABLE 1.—*Interview Material on 200 Enuretics and 200 Nonenuretics*

Item	Percentage and Number of Enuretics	Percentage and Number of Controls	x^2	Probability	Interpretation
Family history of enuresis	69.5% (139)	9.5% (19)	89.62	<0.01	+++
Past history of sleepwalking	34% (68)	10.5% (21)	23.78	<0.01	+++
Family history of sleepwalking	25.5% (51)	10.5% (21)	11.08	<0.01	+++
Family history of epilepsy	Proved*8% (16) Suggestive 1% (2)	2% (4) 0% (0)	6.06	<0.02	++
Past history of epilepsy†	Proved 3% (6) Suggestive 1.5% (3)	0% (0) 0% (0)	–	–	–
History of dental-holding company	19% (38)	10.5% (21)	4.34	<0.04	+

* In the proved cases the subject could give a description of grand mal epilepsy and the affected person had been diagnosed and treated (with daily medication) by a physician. In over one-half of the cases a brain-wave test could be described. In the suggestive cases the patient could describe grand mal seizures but claimed only lay diagnosis without professional confirmation.

† Although the cases are too few to permit treatment by statistical analysis, there is enough case contrast to show a definite trend in the experimental group.

+ Indicates the figures are significant; ++, that they are very significant, and +++, that they are highly significant.

† References 6-12.

‡ Zuska, A. J.; Noble, H. F., and Pierce, C. M.: Unpublished observations.

of sleepwalking. Of the remaining seven (3.5%), two had a past history of sleepwalking, three had a family history of enuresis, two had a family history of epilepsy, and one had a family history of sleepwalking.

There were two other controls who had a family history of epilepsy. One of these men had a sister who walked in her sleep and an epileptic aunt. The mother of the other man was a sleepwalker who had an epileptic brother.

Comment

Hippocrates recognized the familial nature of epilepsy. Aristotle observed the tendency of some epileptics to be stricken in seizure mostly during their sleep. This observation has been confirmed in modern times by many investigators.§

Enuresis, also, has heredofamilial and nocturnal relations. Like epilepsy, enuresis has been known by many clinicians, such as Landau, Oppenheim, Pfister, Janet, and Trousseau, to have familial aspects.‖ The enuretic most commonly exhibits his symptom during his sleep. Some authors have noted that nocturnal enuresis is often found in the person who also suffers various sleep disturbances, such as night terrors or somnambulism.¶ Freud knew that nocturnal enuresis might be a component of an epileptic attack.[25] Gowers described the case of an epileptic girl who could abort a frank seizure only if she could urinate after an aura in her right great toe which traversed upward to the groin.[15] The alienist is aware of the possibility of murder by the sleepwalker, who then remains amnesic for the offense.[26] Such a case is indistinguishable from psychomotor epilepsy.

Thus, historically, there is an abundance of reasoning which links epilepsy to enuresis and somnambulism. The present study presents quantitative data which imply that there is a true biologic basis for this linkage. Presently, one use of such a linkage lies in the possibility that in selected case material enuresis research may serve as an indirect tool in learning more of epilepsy. For example, enuresis is more easily studied since electrical devices may be modified so that the investigator can be notified at the precise instance of the "seizure."# This would simplify the collection of comparative metabolic data before, during, and after an attack.

In considering a family history of enuresis, one is daunted immediately by the possibility that sociocultural influences are the chief factors involved. Such possibilities as family acceptance of the habit or poverty (which results in a cold home or outdoor facilities) could discourage many members of the family in developing adequate vesicle control. The psychological problems resulting in a "P - - - on you" attitude or inadequate bladder training similarly would affect many family members. Nevertheless, many workers have believed that the familial aspects of enuresis often have an organic foundation, compounded by psychodynamic factors and sociocultural situations.* Frary has hypothesized that a recessive gene substitution is active in the etiology of enuresis.[37]

It is common to learn from recruit sentries that they have witnessed a sleepwalker go to the toilet and urinate. Many enuretics and sleepwalkers have knowledge of this type of experience, as well as the experience of believing they have walked to the toilet, when in actuality they are dreaming and committing an enuretic act.† Facts of this sort lend weight to the supposition that enuresis and sleepwalking have a common denominator. Another common denominator is the increased family history of sleepwalking among both enuretics and sleepwalkers. During somnambulistic episodes some sleepwalkers experience déjà vu phenomena.‡

The experimental group in this study has

§ References 15-21.
‖ References 5 and 22.
¶ References 22-24.
# References 27-29.
* References 31-36.
† References 1-4.
‡ References 2, 4.

a more frequent past and family history of epilepsy. These are cases only which manifest overt grand mal epilepsy. Further study must be made on inherited brain patterns of enuretics, as has been done in epileptics.§ Future scrutiny may reveal a more frequent family history of all types of epilepsy in the enuretics.

Of the control group, all the cases of a family history of epilepsy occurred in men who had some personal or family taint of enuresis or sleepwalking. Since this study was begun, it has been a routine experience to find the same taints in young men who are diagnosed as epileptic. A typical example is the case of a 27-year-old sailor, with nine years of service, who walked in his sleep, apparently for the first time in his life, a few days before the onset of idiopathic grand mal epilepsy. He presented family and past histories of enuresis and a family history of post-traumatic epilepsy (in a brother). An unsubstantiated clinical impression is that a family or past history of enuresis and/or sleepwalking may be at least as common in idiopathic epilepsy (in servicemen) as is aura, tongue biting during convulsions, incontinence during convulsions, or a known family history of epilepsy. Accordingly, a history of enuresis or sleepwalking, either past or familial, has become clinically useful in arriving at a diagnosis of epilepsy.

Results from the dental inquiry are limited in value because of lack of correlation with information regarding the subject's economic circumstances, availability to a dentist, diet, family attitude toward dental care, and exact dental diagnosis. Yet the data do show a significant inclination with unfavorable reflection upon the experimental group.

The problem of diet is especially interesting, since controversy rages as to the reason for decreased caries in malnourished populations. Such a reduction may represent lower carbohydrate intake. Yet one wonders if this is the entire cause, for people with less income may eat proportionately more carbohydrate, since it is cheaper. In the quest for an abnormal blood chemical element in epilepsy, socioeconomic and clinical studies of malnourished populations might indicate research leads.

Therefore, for research purposes, controlled studies on dental pathology in epileptics and enuretics might provide hints to the understanding of the biochemistry and physiology of calcium, potassium, and acetylcholine. Likewise, in the cases of enuresis definitely thought to be on the basis of genitourinary pathology,‖ more thorough chemical, dental, and electroencephalographic studies should be contemplated, in view of the known ability of central nervous system irritants to cause dental and bladder pathology. Such drugs as bulbocapnine, which are celebrated for their epileptogenic potency, should be evaluated for their ability to produce dental and genitourinary lesions. Similar efforts to produce these lesions should be made by both electrical and chemical stimulation at specific brain sites. In the same manner anticholinesterase drugs, such as physostigmine, isoflurophate (DFP), nicotine, and strychnine, should be evaluated.

Table 2 compares some clinical features of epilepsy, enuresis, and somnambulism and thereby reveals areas where further investigations are needed. The more the enuretic is compared with the epileptic, the more clearly associated to the epileptic does he become. It would seem that some cases of enuresis and sleepwalking are disorders more "allied" to epilepsy than to migraine, other types of sleep disturbances, or behavior disorders.

It should be mentioned that 18 (9%) of the enuretics and 4 (2%) of the controls were Negroes. This may be important information, since some workers have believed that Negroes have enuresis more frequently than Caucasians,[43] and some case reports note that Negroes are extremely prone to have sleep disturbances sometimes "allied"

§ References 38-39.

‖ References 40-42.

TABLE 2.—*Clinical Relations of Epilepsy, Enuresis, and Sleepwalking*

Relation	Epilepsy	Enuresis	Sleepwalking
1. May occur in association with sleep	Frequently[15]	Usually[5]	Always[1]
2. Paroxysmal recurrence	+[47]	+[5]	+[1]
3. Cerebral dysrhythmia as reflected by EEG	+[47]	+[1]	+[1]
4. Likely to occur in relation to increased emotional stress	+[15]	+[1]	+[1]
5. Attack may be accompanied by phenomenon of déjà vu	+[47]	+[1]	+[1]
6. Automatic behavior during attack	+[47]	?	+[1]
7. May result in postictal amnesia, stupor, or confusion	+[47]	?[5]	+[1]
8. Postictal sleep	Frequently[47]	Usually[5]	Usually[1]
9. Relative cerebral anoxia before, during, and after seizure	Probably +[48]	?	?
10. Attack may be associated with change in sleep depth	Probably +[18]	Probably +[18]	Probably +[1]
11. Therapeutic response to anticonvulsants	+[47]	?	?
12. Increased "normal range" spectrum in biochemical responses	+[6]	?	?
13. May "grow out" of condition	+[47]	+[5]	+†
14. Increased chance of family history	+[39]	+[1]	+[1]
15. Increased chance of family history of one or both of other syndromes	?	+[1]	+[1]
16. Increased chance of past history of one or both of other syndromes	?	+[1]	+[1]
17. May show qualitative urinary abnormalities	Sometimes[14]	Often[1]	?
18. May show quantitative urinary abnormalities	?	Sometimes[24]	?
19. May have more complaints referable to genitourinary system	?	+[1]	+[6]

[5] Nearly always the enuretic alleges inability to tell when he has bed-wet. He states; "I don't know.....I sleep right through." Since the wet bed would serve as sufficient stimulus to arouse most persons, the enuretic may have a defect in central nervous system function which results his failing to awaken. Some investigators believe that failure to awaken is due to inadequate training, poor habits, or psychic conflicts.

† References 2, 57.

to epilepsy.¶ However, before interpretation, the present data must be expanded to make careful allowance for per capita considerations. With respect to general economic status, these youths, like the majority of the Caucasians in the experimental group, were poor Southerners. Again, the sociocultural and economic factors must be considered.

At present we believe that in adolescent male enuretics enuresis is a symptom which has a large organic basis and which has been perpetuated by psychologic deficits. Psychodynamically, the recruit enuretic appears to be the teen-aged youth who grew up from boyhood as a passive, infantile, and sensitive child enuretic.# We think that in many of the cases of enuresis which ceases by puberty the disorder is more usually the result of adverse environmental, training, and psychic conditions. These same conditions operate in the case of the adolescent enuretic, who, to lose his habit, must overcome a larger organic handicap. Clinically, this handicap manifests itself by abnormal brain potentials, a past history of sleepwalking, and a family history of enuresis, sleepwalking, or epilepsy. The patient is a chronic enuretic, often with multiple complaints in the genitourinary system review. Qualitative urinary disturbance may be found upon laboratory analysis.

Electroencephalographic maturation is normally delayed until about the age of 19.[49] There must be chemical correlations to this maturation process. Perhaps the repeated history obtained from adolescent enuretics that they are "growing out" of their enuresis, just as their near relatives did by about the age of 20, may have in fact a physical reason. More intense study is needed on the older adult enuretic and the adolescent female enuretic. Most of the medical literature on the subject deals with

¶ References 44-45.

References 3, 48.

the problem in childhood. This may be a different sort of a problem because of easier social acceptance of the difficulty by the patient and his family, lack of discouragement concerning a cure, and, above all, frequently relatively less central nervous system involvement.

The answers to some of the questions about the relationships of enuresis, epilepsy, and sleepwalking must await a response to the oft-called plea for more knowledge of the metabolism of sleep* and the mechanisms of consciousness.† A start has been made on learning more of the factors which regulate the rhythm of fits in both males and females.[55]

Summary

In the course of a series of exploratory studies designed to provide further avenues for therapeutic and theoretic research into symptomatic immaturity habits, it becomes necessary to elaborate the clinical relationships of enuresis, somnambulism, epilepsy, and poor quality of dentition.

The findings after interview with 200 enuretics and 200 controls show that the enuretic has a statistically significantly greater family and past history of enuresis, sleepwalking, and epilepsy and a greater past history of epilepsy. The enuretic is more likely to have inferior dentition.

Theoretically, in some cases, epilepsy, enuresis, and somnambulism may represent different manifestations of a similar biophysical aberrancy. This abnormality may have been genetically determined and result in "seizures" as a consequence of pathophysiologic changes during sleep which are influenced by emotional duress. The research implications and diagnostic use of such a relationship are discussed.

REFERENCES

1. Pierce, C. M.; Lipcon, H. H.; McLary, J. H., and Noble, H. F.: Enuresis: Clinical, Laboratory and Electroencephalographic Studies, U. S. Armed Forces M. J. 7:208-219 (Feb.) 1956.

2. Pierce, C. M., and Lipcon, H. H.: Somnambulism: Psychiatric Interviews, U. S. Armed Forces M. J., to be published.

3. Pierce, C. M.; Lipcon, H. H.; McLary, J. H., and Noble, H. F.: Enuresis: Psychiatric Interview Studies, U. S. Armed Forces M. J., to be published.

4. Pierce, C. M.; Lipcon, H. H.; McLary, J. H., and Noble, H. F.: Somnambulism: Electroencephalographic and Related Findings, U. S. Armed Forces M. J., to be published.

5. Wilson, S. A. K.: Neurology, Baltimore, William Wood & Company, 1940, Vol. 2.

6. Goldstein, H., and McFarland, R. A.: The Biochemistry of Epilepsy, Am. J. Psychiat. 96:772-850 (Jan.) 1940.

7. Jasper, H. H.: Electrical Activity of the Brain, Ann. Rev. Physiol. 3:377-398, 1941.

8. Lennox, M. A., and Lennox, W. G.: Electrical Activity of the Brain, Ann. Rev. Physiol. 9:507-524, 1947.

9. Brown, M. R.: Paroxysmal Cerebral Dysrhythmia Following Large Doses of Potassium Chloride, Arch. Neurol. & Psychiat. 60:301-302 (Sept.) 1948.

10. Lloyd, D. P., and McIntyre, A. K.: Bioelectrical Potentials, Ann. Rev. Physiol. 11:173-198, 1949.

11. Elliott, K. A. C.: Biochemical Approaches in the Study of Epilepsy, Electroencephalog. & Clin. Neurophysiol. 1:29-31 (Feb.) 1949.

12. Kesel, R.: Caries of Enamel: Evidence for Decalcification Theory, J. Am. Dent. A. 37:381-390 (Oct.) 1948.

13. Miller, S. C., and Firestone, J. M.: Psychosomatic Factors in the Etiology of Periodontal Disease, Am. J. Orthodontics (Oral Surg. Sect.) 33:675-686 (Sept.) 1947.

14. Creevy, C. D.: Neurogenic Vesical Dysfunction: Alterations in Physiology of Micturition Due Lesions of Nervous System, Arch. Neurol. & Psychiat. 34:777-802 (Oct.) 1935.

15. Gowers, W. R.: Epilepsy, Ed. 2, London, J. & A. Churchill, Ltd., 1901.

16. Langdon-Down, M., and Brain, W. R.: Time of Day in Relation to Convulsions in Epilepsy, Lancet 1:1029-1032 (May 18) 1929.

17. Patry, F. L.: The Relation of Time of Day, Sleep and Other Factors to the Incidence of Epileptic Seizures, Am. J. Psychiat. 87:789-813 (March) 1931.

18. Hopkins, H.: The Time of Appearance of Epileptic Seizures in Relation to Age, Duration and Type of the Syndrome, J. Nerv. & Ment. Dis. 77: 153-162 (Feb.) 1933.

19. Magnussen, G.: Eighteen Cases of Epilepsy with Fits in Relation to Sleep, Acta psychiat. et neurol. 11:289-321, 1936.

20. Abbott, J. A., and Schwab, R. S.: Some Clinical Aspects of the Normal Electroencephalo-

* References 48-51.

† References 52-54.

gram in Epilepsy, New England J. Med. 238:457-461 (April 1) 1948.

21. Caveness, W.; Parsonage, M., and Edmond, M.: Convulsive Seizures Coincident with Sleep, Tr. Am. Neurol. A. 75:155-159, 1950.

22. Glicklich, L. B.: Historical Account of Enuresis, Pediatrics 8:859-876 (Dec.) 1951.

23. Levine, A.: Enuresis in the Navy, Am. J. Psychiat. 100:320-325 (Nov.) 1943.

24. Berdie, R. F., and Wallen, R.: Some Psychological Aspects of Enuresis in Adult Males, Am. J. Orthopsychiat. 15:153-159 (Jan.) 1945.

25. Freud, S.: The Basic Writings of Sigmund Freud, translated and edited by A. A. Brill, New York, Random House, Inc., 1938.

26. Hopwood, J. S., and Snell, H. K.: Amnesia in Relation to Crime, J. Ment. Sc. 79:27-41 (Jan.) 1933.

27. Mowrer, O. H., and Mowrer, W. M.: Enuresis: A Method for Its Study and Treatment, Am. J. Orthopsychiat. 8:436-459 (July) 1938.

28. Davidson, J. R., and Douglass, E.: Nocturnal Enuresis: A Special Approach to Treatment, Brit. M. J. 1:1345-1347 (June 10) 1950.

29. Seiger, H. W.: Treatment of Essential Enuresis, J. Pediat. 40:738-749 (June) 1952.

30. Anderson, F.: Psychiatric Aspects of Enuresis, Am. J. Dis. Child. 40:591-618 (Sept.) 1930; 818-843 (Oct.) 1930.

31. Usher, S. J.: The Treatment of Enuresis in Hospital Practice, Canad. M. A. J. 24:665-667 (May) 1931.

32. Stockwell, A. L., and Smith, C. K.: Enuresis: A Study of Causes, Types and Therapeutic Results, Am. J. Dis. Child. 59:1013-1033 (May) 1940.

33. Thorne, F. C.: The Incidence of Nocturnal Enuresis After Age 5, Am. J. Psychiat. 100:686-689 (March) 1944.

34. Backus, P. L., and Mansell, G. S.: Investigation and Treatment of Enuresis in the Army, Brit. M. J. 2:462-465 (Oct. 7) 1944.

35. Cattell, J. P., and Pacella, B. L.: An Electroencephalographic and Clinical Study of Children with Primary Behavior Disorder, Am. J. Psychiat. 107:25-33 (July) 1950.

36. Turton, E. C., and Spear, A. B.: EEG Findings in 100 Cases of Severe Enuresis, Arch. Dis. Childhood 28:316-320 (Aug.) 1953.

37. Frary, L.: Enuresis: Genetic Study, Am. J. Dis. Child. 49:557-578 (March) 1935.

38. Lennox, W. G.; Gibbs, E. L., and Gibbs, F. A.: Inheritance of Cerebral Dysrhythmia, Arch. Neurol. & Psychiat. 44:1155-1183 (Dec.) 1940.

39. Lennox, W. G.: The Genetics of Epilepsy, Am. J. Psychiat. 103:457-462 (Jan.) 1947.

40. Campbell, M. F.: Enuresis, Arch. Pediat. 54: 187-197 (April) 1937.

41. Winsbury-White, H. P.: A Study of 310 Cases of Enuresis Treated by Urethral Dilatation, Brit. J. Urol. 13:149-162 (Sept.) 1941.

42. Abernathy, A. C., and Tomlin, E. M.: Treatment of Enuresis in Female Children, J. Urol. 72: 1163-1166 (Dec.) 1954.

43. Bakwin, H.: Enuresis in Children, J. Pediat. 12:757-768 (June) 1938.

44. Cohn, R., and Cruvant, B.: Relation of Narcolepsy to the Epilepsies, Arch. Neurol. & Psychiat. 51:163-170 (Feb.) 1944.

45. Solomon, P.: Narcolepsy in Negroes, Dis. Nerv. System 6:179-183 (June) 1945.

46. Gerard, M. W.: Enuresis: A Study in Etiology, Am. J. Orthopsychiat. 9:48-58 (Jan.) 1939.

47. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., Addison-Wesley Press, 1952, Vol. 2.

48. MacWilliam, J. A.: Some Applications of Physiology to Medicine: III. Blood Pressure and Heart Action in Sleep and Dreams, Brit. M. J. 2:1196-1200 (Dec. 22) 1923.

49. Kleitman, N.; Cooperman, N. R., and Mullin, F. J.: Studies on the Physiology of Sleep: IX. Motility and Body Temperature During Sleep, Am. J. Physiol. 105:574-584 (Sept.) 1933.

50. Brain, R.: Sleep: Normal and Pathological, Brit. M. J. 2:51-53 (July 8) 1939.

51. Vaisrub, S.: Nocturnal Disorders of Medical Interest, Ann. Int. Med. 35:323-330 (Aug.) 1951.

52. Magoun, H. W.: Caudal and Cephalic Influences on Brain Stem Reticular Formation, Physiol. Rev. 30:459-474 (Oct.) 1950.

53. Lovett Doust, J. W., and Schneider, R. A.: Studies on the Physiology of Awareness: Anoxia and Levels of Sleep, Brit. M. J. 1:449-455 (March 1) 1952.

54. Cobb, S.: Progress in Internal Medicine: Review of Neuropsychiatry, A. M. A. Arch. Int. Med. 95:129-136 (Jan.) 1955.

55. Almqvist, R.: The Rhythm of Epileptic Attacks and Its Relation to the Menstrual Cycle, Acta psychiat. et neurol. scandinav., Supp. 105, 1955.

56. Davis, E. W.; McCulloch, W., and Roseman, E.: Rapid Changes in the Oxygen Tension of Cerebral Cortex During Induced Convulsions, Am. J. Psychiat. 100:825-829 (May) 1944.

57. Rottersman, W.: Selectee and His Complaints, Am. J. Psychiat. 103:79-86 (July) 1946.

58. Ditman, K. S., and Blinn, K. A.: Sleep Levels in Enuresis, Am. J. Psychiat. 111:913-920 (June) 1955.

Homeostasis and Personality

HARRY A. TEITELBAUM, M.D., Ph.D., Baltimore

Man's intricate integration with his environment is not a haphazard process. His constituent biologic systems are maintained within a narrow range of fluctuation by a self-regulating homeostasis, as so vividly portrayed by Cannon.[7] How an organism's behavior is motivated to compensate for deficits resulting from homeostatic failure has been clearly established experimentally by Richter.* Even in the complexities of modern society does homeostasis play a regulating role, according to Cannon.[7] Ashby[3] remarked that civilization's advantages are the results of the limiting effects of homeostasis on variation, and Emerson[11] stressed the homeostatic social regulation of the diverse aspects of our civilization, such as architecture, agriculture, economics, and public health.

The complex experimental data on organism homeostasis have been interpreted by Hoagland,[18] by Hill,[17] and particularly by von Bertalanffy,[37] in the light of our understanding of inorganic thermodynamic processes. This has given rise to the fundamental thesis that living organisms are never in actual equilibrium, and that this lack of equilibrium is the result of homeostasis. When homeostatic failure occurs, then the organism goes into thermodynamic equilibrium with its environment; or, to put it more simply, it dies. The organism becomes an inorganic system and reacts like other inorganic systems.

Any living creature can be fully understood only when viewed holistically in relation to its changing environment. In addition, it should be considered as a hierarchy of organism-environment systems, those that are less complex being lower in this hierarchy than those that are more complex, as defined so well by Novikoff.[26] The more complex systems result from the integration of those that are less complex with one another. In accord with this concept, Aldrich[2] discusses emotional homeostasis in personality adaptation as occurring on a number of levels.

Accepted for publication April 6, 1956.

* References 27, 29.

Homeostasis in the Nervous System

In the higher forms of animal life, it is the nervous system that makes communication with the environment possible. Breuer and Freud[6] interpreted the function of the nervous system in various aspects of behavior on the basis of principles now readily recognized as homeostatic. They stressed the "tendency of the organism to preserve a constant level of tonic cerebral excitement" in the light of the "need (to) be fulfilled." That neurologic integrative processes involve homeostatic feed-back mechanisms, in bringing about an adequate organism-environment adaptation, is well known. Gellhorn[15] presents a very detailed and stimulating discussion of this problem.

Teitelbaum,[34] Fessard,[13] and others stress the importance of the hierarchy of integrative processes in the nervous system. The highest-order integrative processes in the neurologic hierarchy are those involving the more complex functions of the cerebral cortex, those representing the "apprehension of values and meanings" being at the apex, according to Fessard.[13] The neurone-impulse integrative configurations or circuits that make up neurologic homeostatic systems function as regulating processes that correct behavior to the degree that the organism fails to achieve its environmental goals. This is accomplished by the feed-back of neural discharges that are deter-

mined by the degree to which the intended goals are not being achieved, with the effect that the central regulating processes of the nervous system automatically alter behavior in a manner that makes the goals more attainable. For instance, in driving a car the visual evaluation of one's distance from surrounding objects automatically adjusts the degree to which one steps on or releases pressure from the accelerator.

Homeostasis in Mobilization and Motivation Processes

In the consideration of homeostasis, accent is usually placed on the limited range of fluctuation that is achieved in the various organism systems, such as that of body temperature, etc. I should like to concentrate on an interpretation of homeostasis that stresses, not this limited range of fluctuation, but, rather, the processes of mobilization and motivation that bring into play the integrative functions which prevent any excessive fluctuation. Aldrich [2] calls attention to the simpler, lower-level mobilization functions in personality adaptation, but with regard to the higher levels he merely refers to voluntary and involuntary adaptation.

In the organism-environment hierarchy referred to above, the homeostasis of such systems as those of body temperature and fluid balance are at a relatively low level in comparison with personality homeostasis, which refers to the behavior of the total organism involved in the attainment of reality goals in a complex social environment. Excessive fluctuation in lower-level homeostasis is prevented primarily by *mobilization* processes. As an example, when one is hot, the lower-order homeostatic integrative processes that maintain body temperature are *mobilized* to bring about the dilatation of peripheral blood vessels, excretion of sweat, etc. If mobilization fails to reestablish homeostasis, then *motivation* processes are activated. Thus, to continue with the above example, when mobilization is inadequate, one is *motivated* to take off one's coat; to mix a refreshing mint julep, as done in Kentucky, or to drink hot tea and then fan oneself, as done in China, to maintain constant body temperature. In this sense, excessive fluctuation in behavior that interferes with the attainment of environmental goals at the level of personality brings motivation processes into play. In this hierarchy the less complex mobilization processes of the lower-order homeostatic systems of the organism-environment hierarchy are further integrated into the more complex motivation processes of the higher-order homeostatic systems involved in personality adjustment. In their most refined forms the motivation processes involve the awareness and attainment of reality goals.

It is particularly when lower-order mobilization functions fail to maintain the end-processes of the various systems within their optimum range of fluctuation that the higher-order motivation processes become clearly evident. Thus, in Richter's † hypophysectomized or thyroidectomized rats, with the failure of mobilization of endocrine integration that maintains body temperature there was motivation of organism-environment integration, with the resultant complex activity of gathering available paper to build nests. The amount of paper used varied inversely with the environmental temperature. Richter's [28] data on self-selection of diets in the face of deficiencies resulting from surgically imposed endocrine inadequacies are well known, and prove again the motivating effects of disturbed homeostasis. Similarly motivated behavior was reported clinically by Wilkins and Richter [39] in a child with adrenal cortex deficiency who craved salt and resorted to every possible measure to obtain it. This child, like the rats, was motivated by disturbed homeostasis that could not be corrected by lower-order mobilization processes, to adaptive activity that reestablished homeostasis. With regard to the processes involved in the growth of the various civilizations, Toynbee [36] refers to the Eskimos as an arrested civilization. This is due to the great stress

† References 27-29.

imposed on them by the Arctic climate. Their behavior is primarily motivated by the need to maintain lower-order homeostasis, so that little energy or time is available for further cultural development. This is not unlike the behavior of Richter's rats, and of his adrenal-cortex-deficient boy, who was motivated by the need to maintain lower-order homeostasis.

The basic psychophysiological law I should like to formulate is that at the highest level in the hierarchy of personality (organism-environment integration) motivation results from excessive fluctuation beyond the optimum range of homeostatic end-processes. This motivation involves highly complex neurone integrative processes that are experienced as emotional feeling, motor expression, and thought. In mature personalities the effect is behavior that tends to limit the excessive fluctuation of the homeostatic end-processes with the successful attainment of real environmental goals. This formulation is in concordance with Menninger's [23] reference to the ego as "the integrated operation of all homeostatic partial systems—physiological and psychological — which comprise the total personality." It stands in contrast to Nielsen and Thompson's [25] concept that "conation is the inherent urge to move, the most fundamental of cerebral functions." French [14] stands opposed to such a circumscribed concept. He maintains that the mere study of cerebral processes is inadequate for the understanding of "the integrative mechanisms that make motivated behavior possible." Motivation is, as suggested above, the result of excessive disturbance in higher- as well as in lower-level homeostatic systems in the hierarchy of personality (organism-environment integration).

Homeostasis and Psychopathological Processes

An understanding of homeostasis also affords a good basis for the comprehension of abnormal processes. Homeostatic failures result in physiopathological and psychopathological effects involving the respective levels in the hierarchy of personality. It is in these disturbed conditions that the integrative mobilization and motivation processes undergo disintegration and may then suffer faulty reintegration, which gives rise to the various physiological and psychopathological defensive reactions.

Selye [31] touches upon Claude Bernard's and Cannon's homeostatic concepts in his studies of stress. These studies clearly imply that under marked stress an organism undergoes homeostatic disruption, with the development of the "alarm reaction" and the "phase of shock." This may lead to death or to the defensive "phase of counter-shock." This phase I interpret as involving the reintegration of homeostasis through the activity of the diverse mobilization and motivation processes.

To express Selye's views in terms of my basic formulation, I should consider his shock phase as an extensive disruption of homeostasis, with resultant physiological disturbances, as well as associated disturbance in emotional feeling, motor expression, and thinking. These disturbances mobilize and motivate, at respective levels in the hierarchy of personality, the reintegration of homeostasis. This reintegration is the equivalent of Selye's countershock phase, in which there occurs a "reversal of most of the changes seen during the shock phase." Whether the results of reintegration are normal or abnormal depends on a variety of factors, too complex to discuss here in detail.

Continuing with the interpretation of Selye's data in terms of homeostasis, his "general adaptation syndrome" or "diseases of adaptation" refer to abnormally reintegrated homeostasis, for they are, as Selye [31] puts it, "maladies referable to an abnormality of the adaptation-process itself, to maladaptation." Homeostasis is the major adaptation mechanism whereby an organism maintains its integrity in a changing environment.

Selye [31] makes slight reference to psychological processes. He mentions the complicated nature of psychosomatic mech-

anisms in the general adaptation syndrome and decries the failure to study adequately the psychological aspects of adaptation to stress. This criticism is not warranted, for the broad area of the psychopathology of defenses in personality integration really involves psychogenic diseases of adaptation to stress. The rigid defenses of a schizoid person, or of an obsessive-compulsive neurotic, are maladaptations. These defenses are abnormal reintegrative processes resulting from the motivating effects of disturbing stressful experiences.

Along the lines of the above discussion, Stern [32] has employed Selye's [31] views in explaining the dynamics of symptom formation. He refers to Selye's [31] shock phase as the "catabiotic processes," which "are opposed by regulative (countershock) vital functions." The regulative processes are "anabiotic." Under stress there is a failure of homeostasis, according to Stern,[32] with resultant catabiotic reaction, due to inadequate anabiotic activity. To paraphrase this, under stress there is homeostatic disruption with defective reintegration of the homeostatic adaptive processes and resultant symptom formation. Grinker and Robbins,[16] and several contributors to the volume edited by Deutsch,[9] discuss this aspect of homeostasis. Menninger [23] calls attention to the role of the ego in homeostatic regulatory functions.

Homeostases and Instincts

Not only does homeostasis play a fundamental role in motivation but it also lends itself to a significant interpretation of instincts. In his very interesting paper, Szasz [33] refers to data that support "a unitary instinct theory. The data presented center around present-day biological theories concerning the nature of life processes. Accordingly, the hypothesis is suggested that there is but one primary instinct, a life instinct, the aim of which is to keep the life processes of a particular system in continued operation [or out of thermodynamic equilibrium] and this is accomplished by drawing negative entropy from the environment," as suggested by Schrodinger.[30] Menninger,[23] however, relates thermodynamic equilibrium to the death instinct. While thermodynamic equilibrium of an organism with its environment is equivalent to death, it is difficult to accept thermodynamic processes, which pertain to all inanimate, as well as to animate systems, as instinctive. It would be comparable to claiming that the process of gravitation is instinctive because animate bodies tend to fall. On the contrary, instinctive homeostatic functions involving the righting reflexes, with their proprioceptive feed-back processes, counteract gravity in maintaining an erect position, just as homeostasis counteracts thermodynamic equilibrium, or death.

Without getting involved in a more technical discussion of the homeostatic-thermodynamic interrelationship at this moment, I would like to point out that the feelings associated with disturbed homeostasis include those ascribed to the so-called basic instincts. The drives to breathe, drink, eat, urinate, have sexual intercourse, etc., are instinctive, or the expressions of genetically inherited processes. The homeostatic processes are similarly inherited. The so-called instinct to breathe involves homeostatic integrative, neurohumoral processes, with impairment of which, so that the end-process of oxygen concentration diminishes below the optimum range of variation, the organism experiences the feelings associated with anoxia or asphyxia. If the organism is able to continue to function in an integrated manner, there is lower-order mobilization and higher-order motivation that tend to reestablish the homeostasis of the end-process of oxygen concentration. The same can be said about fluid deprivation or excess, with the respective associated feelings of thirst and congestion, that give rise to appropriate mobilization and motivation to activity that prevents thermodynamic equilibrium, or death. With regard to the so-called sexual instinct, homeostasis exists when, in the well-integrated organism, there is no motivation to practice coitus. When the endocrine homeostasis is disturbed by

an increase in the production of various hormones, as of the pituitary and gonads, feelings associated with the urge for coitus develop and there occurs the mobilization of hormonal and neurone integrative processes, as well as motivation to achieve the environmental goal of coital activity. If successful, this leads to the return of homeostasis and cessation of the feelings evoked, as well as of the activity.

The idea that instincts refer to homeostatic mobilization and motivation integrative processes that preserve life, or prevent the organism from going into thermodynamic equilibrium with its environment, goes along with Szasz' [33] suggestion of "one primary instinct, a life instinct." The sexual instinct which is the motivation or drive to cohabit, is really a suborder integrative system in the hierarchy of personality that maintains species homeostasis. It is similar to the other suborder instincts, such as the instinct to breathe, to eat, to drink, etc. In this sense, Menninger [23] refers to "the somatic ego." He points out that ego function is concerned with physiological, as well as psychological, homeostasis, and that it is "highly artificial to exclude from ego function the recognition of the needs of the body for oxygen, for water," etc.

The hierarchy of personality is constituted of integrative processes of graded degrees of complexity, from the lower-suborder ionic and molecular systems, to higher-order neurone-impulse integrative systems, and then to highest-order psychological processes involving emotional feeling and expression, as well as intellectual processes. This hierarchial concept is applicable to homeostatic integrative processes, as well as to instincts, which, as formulated above, refer to these very homeostatic processes. In this sense Fenichel [12] writes, "Homeostasis is as a principle at the root of all instinctual behavior." These views are quite like those expressed by Kubie,[21] in which he ascribes three components to the various instincts. These are "a biochemical core, a network of neurones and neuronal synapses and a psychologic superstructure. The difference that remains will appear as one of degree rather than of kind." While Kubie [21] uses the above formulation to show that there is no distinction between an instinctual act and a drive, we see here the essence of the various suborder homeostatic integrative systems, molecular, neurologic, and psychological, in the hierarchy of personality. While Kubie [21] stresses that the instincts can be arranged in a hierarchy of increasing complexity, he writes, "It will become clear that all instinctual processes serve either procreative purposes for the species, or else homeostatic and self-regulating functions for the individual." I see no need to isolate procreational processes from the homeostatic, for the former can be understood in terms of the latter at the various degrees of integrative complexity of personality, in the service of species and social adaptations.

I am in full agreement with Kubie's [21] formulation that "the instinctual messages to the brain arise from bodily changes which generate the afferent impulses that impinge on the asynchronous dynamic processes of the central nervous system." These "bodily changes," Kubie [21] points out, refer to homeostasis. He sums up as follows: "In the interrelationship between the self-regulatory activities of simple tissues and organs on the one hand and on the other the regulating functions of integrated behavior problems of the whole organism lies whatever clarification we can bring to the concepts of Instinct." This "clarification," I believe, lies in the concept of a hierarchy, with the "self-regulatory activities of simple tissues and organs" making up lower-order homeostatic integrative systems, and the "integrated behavior problems of the whole organism" making up the highest-order homeostatic integrative systems, involving emotional and psychological processes.

That Kubie [21] does not always apply the hierarchial concept, though he does imply it, is evident in his classification of instincts, as "1) the Primary or Vital Instincts; 2) the Secondary or Sexual Instincts; 3) the

Tertiary or Executive Instincts." The first is concerned with vital processes, as respiration, and it "serves homeostatic functions directly and unmistakably; the role of the second in individual homeostasis is problematical, and the third serves the first two and may in addition have homeostatic functions of its own." The third group mediates "muscular adjustments, alertness and sleep." Thus Kubie [21] conceives of instincts as having or serving homeostatic functions, rather than as being manifestations of homeostatic integrative systems of varying degrees of complexity, ranging from low-order ionic and molecular systems to higher-order neurone-impulse integrative systems, and, finally, to the highest order, involving emotional and psychological processes. In the holistic organism-environment system, these instincts or homeostatic systems keep the organism and species from dying, or from going into thermodynamic equilibrium with its environment.

One of the reasons for the vagueness that enshrouds conventional concepts of instincts is the tendency to think of them as well-defined, fixed mechanisms that function in a rigid, yet rather occult, manner. The established concepts of instincts require reevaluation in the light of those aspects of "the new physics," as stressed by Darwin,[8] which show that "nature has no sharp edges, and if there is a slight fuzziness inherent in absolutely all facts of the world, then we must be wrong if we attempt to draw a picture in hard outline." Similar views have been expressed by Mullahy,[24] who admonishes that "discrete things" are really only "aspects of a field." He stresses that "there has been a change from 'matter' to 'event' or, better, 'process' as a basic category of understanding the world." In the introduction to Huxley's [19] recent essay, Rioch deplores the tendency to accept "a static, completed, absolute concept of the universe, based on authoritarian dogma, rather than recognizing that 'reality is a process.'" He advocates "a unitary form of thinking . . . in terms of organization and process," as propounded by Huxley.[19]

The concept of instincts as presented above is expressed "in terms of organization and process." Instincts are homeostatic integrative processes of diverse degrees of complexity. In the hierarchy of personality they consist of low-order systems that are integrated into higher-order systems, their ultimate integration being into the holistic organism-environment system, or personality. Instincts, or homeostatic processes, maintain organism life, and prevent thermodynamic equilibrium with the environment, on both an individual and a species basis.

In clinical medicine this concept of homeostasis is fully recognized and exploited. The so-called normal values for body temperature, blood glucose, chlorides, etc., are indications of homeostasis. Any deviations in these values from the normal are considered as evidence of illness, and measures are taken to bring the values back to normal, even though in most instances the pathological processes causing the homeostatic disturbances are not clearly understood. Clinically, a diminished temperature is counteracted by extra covers and the use of warming devices. An elevated temperature is lowered by means of alcohol sponges and antipyretic drugs, as acetylsalycylic acid. Low blood sugar is counteracted by increased glucose intake, and an excess of blood glucose is lowered by dietary restrictions or insulin administration. Thus, often, even though the pathology causing the disturbances in the homeostasis is not corrected, the maintenance of the end-processes within the optimum range of fluctuation keeps the organism alive. It is thus apparent that many diseases are fatal to the organism because they impair its lower-order instinctive, or homeostatic, functions. Patients have been reported, and I have witnessed such cases, with seemingly nonfatal pathology, but with complete lack of desire to live, who have died despite all efforts to save them. In such cases the absence of motivation to survive implies complete disintegra-

tion of high-order personality homeostasis. Formerly healthy wild animals sometimes die in confinement as a result of a similar lack of motivation to maintain organism-environment homeostasis.

Summary

Personality consists of a hierarchy of homeostatic processes of graded degrees of complexity, those that are lower in this hierarchy, or less complex, being integrated into the higher, or more complex, processes. Personality considered as a holistic organism-environment system is at the apex of this hierarchy.

Homeostasis, a self-regulating, feed-back process, is commonly considered from the point of view of its tendency to prevent fluctuation, beyond an optimum range, of the end-processes of the constituent systems of an organism, and thus of the organism as a whole, despite marked variations in the environment. Without minimizing the significance of this manner of viewing homeostasis, attention is directed to the *process of mobilization* that brings into play those integrative functions that prevent excessive fluctuation in the end-processes of the lower-level systems, as of body temperature. Mobilization of these integrative functions is brought about when excessive fluctuation in these end-processes occurs. The mobilization processes are of a low order in the hierarchy of personality, and by further integration they give rise to higher-order *motivation* processes. Thus, when there is excessive fluctuation beyond the optimum range of the more complex homeostatic processes in the hierarchy of personality, the motivation processes function so as to reestablish homeostasis. Also, the higher-order motivation processes become activated when the lower-order mobilization processes fail to reestablish homeostasis in lower-order systems. Motivation involves highly complex neurone-impulse integrative processes that are experienced as emotional feeling and expression, as well as thought. It leads to behavior that tends to reestablish lower-order, as well as highest-order, personality homeostasis by means of multiple neural feed-back discharges which facilitate the attainment of environmental goals.

Homeostasis affords a good basis for the understanding of personality aberrations. Not only are homeostatic failures the basis for physiopathological and psychopathological processes involving the respective orders in the hierarchy of personality, but also the integrative mobilization and motivation processes that maintain homeostasis are subject to distintegration, as well as to faulty reintegration, with resultant physio- and psychopathological defensive reactions. The above formulation is applicable to the response of the organism to stress, as described by Selye,[31] and his diseases of adaptation can be considered as lower-order processes, of which the higher-order counterparts are the personality defenses, which may be psychopathological, and thus defective adaptations to stress.

A unitary concept of instincts, stressing the validity of one instinct involving the maintenance of life, is suggested. In this concept homeostatic and instinctive processes are considered as equivalents.

1801 Eutaw Pl. (17).

REFERENCES

1. Adrian, E. D.: The Physical Background of Perception, London, Oxford University Press, 1946.

2. Aldrich, C. K.: Psychiatry for the Family Physician, New York, McGraw-Hill Book Company, Inc., 1955.

3. Ashby, W. R.: Design for a Brain, New York, John Wiley & Sons, Inc., 1952.

4. Brain, W. R.: Mind, Perception and Science, Springfield, Ill., Charles C Thomas, Publisher, 1951.

5. Brazier, M. A. B.: Neural Nets and the Integration of Behavior, in Perspectives in Psychiatry, D. Richter, Editor, London, H. K. Lewis & Co., Ltd., 1950, pp. 35-46.

6. Breuer, J., and Freud, S.: Studies in Hysteria, Nervous and Mental Disease Monographs, 1950.

7. Cannon, W. B.: The Wisdom of the Body, New York, W. W. Norton & Company, Inc., 1939.

8. Darwin, C. G.: Logic and Probability in Physics, Phil. Sc. 6:48, 1939.

9. Deutsch, F.: The Psychosomatic Concept in Psychoanalysis, New York, International Universities Press, 1953.

10. Eccles, J. C.: The Neurophysiological Basis of Mind: The Principles of Neurophysiology, London, Oxford University Press, 1953.

11. Emerson, A. E.: Dynamic Homeostasis: A Unifying Principle in Organic, Social and Ethical Evolution. Scient. Month. 77:67-85, 1954.

12. Fenichel, O.: The Psychoanalytic Theory of Neurosis, New York, W. W. Norton & Company, Inc., 1945.

13. Fessard, A. E., in Mechanisms of Nervous Integration and Conscious Experience, E. D. Adrian, F. Bremer, and H. H. Jasper, Editors, Springfield, Ill., Charles C Thomas, Publisher, 1954, pp. 200-235.

14. French, T. M.: The Integration of Behavior, in Basic Postulates, Chicago, University of Chicago Press, Vol. I, 1952.

15. Gellhorn, E.: Physiological Foundations of Neurology and Psychiatry, Minneapolis, University of Minnesota Press, 1953.

16. Grinker, R. R., and Robbins, F. P.: Psychosomatic Case Book, New York, Blakiston Division of McGraw-Hill Book Company, Inc., 1954.

17. Hill, A. V.: Adventures in Biophysics, Philadelphia, University of Pennsylvania Press, 1931.

18. Hoagland, H.: Pacemakers in Relation to Aspects of Behavior, New York, The Macmillan Company, 1935.

19. Huxley, J.: Knowledge, Morality, and Destiny, Psychiatry 14:127, 1951.

20. Konorski, J.: Conditioned Reflexes and Neuron Organization, London, Cambridge University Press, 1948.

21. Kubie, L. S.: Instincts and Homeostasis, Psychosom. Med. 10:15, 1948.

22. McCulloch, W. S.: Modes of Functional Organization of the Cerebral Cortex, Fed. Proc. 6:448-452, 1947.

23. Menninger, K. A.: Psychological Aspects of the Organism Under Stress: 1. The Homeostatic Regulatory Function of the Ego, J. Am. Psychoanalyt. A. 2:67, 1954.

24. Mullahy, P.: A Philosophy of Personality, Psychiatry 13:417, 1950.

25. Nielsen, J. M., and Thompson, G. N.: The Engrammes of Psychiatry, Springfield, Ill., Charles C Thomas, Publisher, 1947.

26. Novikoff, A. B.: The Concept of Integrative Levels and Biology, Science 101:209-215, 1945.

27. Richter, C. P.: Biology of Drives, Psychosom. Med. 3:105, 1941.

28. Richter, C. P.: The Self-Selection of Diets, in Essays in Biology, in honor of Herbert M. Evans, Berkeley, Calif., University of California Press, 1943, pp. 501-506.

29. Richter, C. P.: Biology of Drives, J. Comp. Physiol. 40:129, 1947.

30. Schrodinger, E.: What Is Life? New York, The Macmillan Company, 1947.

31. Selye, H.: The Physiology and Pathology of Exposure to Stress, Montreal, Canada, Acta, Inc., 1950.

32. Stern, M. M.: Trauma and Symptom Formation, Internat. J. Psycho-Analysis 34:202, 1953.

33. Szasz, T. S.: On the Psychoanalytic Theory of Instincts, Psychoanalyt. Quart. 21:25, 1952.

34. Teitelbaum, H. A.: The Role of the Cerebral Cortex in the Dynamics of Personality as a Holistic Organism-Environment System, J. Nerv. & Ment. Dis. 115:489, 1952.

35. Teitelbaum, H. A.: The Rhythmic Activity of the Nervous System, Phil. Sc. 20:42, 1953.

36. Toynbee, A. J.: A Study of History, Abridgement of Vols. 1-6, by D. C. Somervell, New York, Oxford University Press, 1947.

37. von Bertalanffy, L.: Problems of Life: An Evaluation of Modern Biological Thought, New York, John Wiley & Sons, Inc., 1952.

38. von Bonin, G.: Essay on the Cerebral Cortex, Springfield, Ill., Charles C Thomas, Publisher, 1950.

39. Wilkins, L., and Richter, C. P.: Great Craving for Salt by Child with Cortico-Adrenal Insufficiency, J. A. M. A. 114:866-68, 1940.

Studies in Itching

II. Some Psychological Implications of the Interrelationships Between the Cutaneous Pain and Touch Systems

JOSEPH G. KEPECS, M.D.
and
MILTON ROBIN, M.D., Chicago

The skin is a particularly fortunate site for studying certain peripheral manifestations of the functioning of the psychic structures originally described by Freud. Indeed, we might say that in a phylogenetic sense the skin is the mother structure of both the id and the ego. "The skin, which in particular parts of the body has become differentiated into sense organs or modified into mucous membrane, and is thus the erotogenic zone *par excellence*."[5] "The ego is first and foremost a body-ego; it is not merely a surface entity, but is itself the projection of a surface."[4] An authorized note by the translator amplifies this statement: "The ego is ultimately derived from bodily sensations, chiefly from those springing from the surface of the body."

The study of sensory and perceptual phenomena in their bearing on the total functioning of the organism is by no means new.[1] The aim of relating studies of perception to clinical psychiatry has been well put by Klein and Schlesinger[13]:

> Rather, we want to use the clinical material in a broader way: to look at the clinical picture of each person and fathom its meanings in terms of his perceptual type. Perhaps clinical material can also help explain differences *within* perceptual types. On the other hand, diagnostic clinical types (e. g., obsessive-compulsive, hysteric, schizoid, etc.) might themselves be directly translated into perceptual hypotheses. For example, hysterical defensive structures, clinically defined, might actually correspond with a quite unique pattern on the perceptual level which contrasts, say, with that to be found for obsessive-compulsives.

Studies of this type afford a bridge between psychology, psychophysics, and psychoanalysis, for psychophysics objectively measures perceptual responses to physical stimuli, psychology may correlate these observations with the personality of the person being studied, and psychoanalysis attempts to relate both the psychophysical measurements and the psychological classification to its knowledge of the structural, instinctual, and interpersonal aspects of psychic activity. To which we might add that they may also extend and validate a basic intuition of Freud, that there is a biological-physiological substratum which sets the stage, limits, and to an extent defines the various categories and the repertoire of human feelings and behavior.

In a previous paper[12] we studied the sensations produced in the skin by light stroking with cotton wool. The principal subjects were ourselves. We concluded that the pain system of the skin has its own pleasure system, most clearly manifested as tickle. We described a spectrum of increasing degrees of intensity of stimulation of the pain system, from tickle, through itch, to pain. Stimulation of the cutaneous pain system is pleasurable if the intensity of the stimulation is not too great, in the presence of an area of local skin excitation termed itchy skin. Our findings were related to the clinical phenomena of erogenous masochism and to the elucidation of the physiological factors underlying and conditioning masochism. We concluded that the study of sensory physiology may provide us with a further means of investigat-

Received for publication on March 21, 1956.

From the Institute for Psychosomatic and Psychiatric Research and Training of the Michael Reese Hospital.

ing some of our basic psychoanalytic concepts.

We subsequently investigated the responses of a number of patients with dermatoses to stroking with cotton wool. These responses, as might be expected, appear to be related to the personalities of the patients, and perhaps to the course and prognosis of the dermatitis. The principal types of response to stroking with cotton wool are the following:

I. Normal adaptation. Sometime within the two-minute test period the initial sensation of tickle or itch is replaced by a sensation of touch.

II. No adaptation (algedonic response). Throughout the test period only the sensations of tickle or itch are perceived.

III. Touch throughout (analgedonic response). The initial response is a touch sensation, including rubbing, brushing, etc., and this persists unchanged throughout the test period.

IV. Shifting adaptation. Responses tend to alternate between itch or tickle and touch.

V. Partial adaptation. Initial responses of tickle are replaced by touch, but the touch sensation contains a reportable admixture of tickle.

Clinical Data

A pilot study of a number of patients with various dermatoses was undertaken. The patients were tested by cotton-wool stroking. We found, on the basis of a brief clinical interview, that we were generally able to predict whether or not normal adaptation would occur. Patients who appeared emotionally labile tended to show no adaptation. Those who appeared more controlled usually manifested normal adaptation.[1] (This division into labile and controlled corresponds to the division into hysterical and rigid groups that we used in our clinical study of atopic dermatitis.[11]

Report of Cases

Case A.—A 30-year-old single white woman was observed at Cook County Hospital. A detailed psychiatric history was not obtained. She suffers from seborrheic dermatitis. She complains of uncontrollable itching in the pubic region. She emphasizes that she does not worry about herself. She tries to forget her troubles. "It does no good to worry." She is very defensive, and her attitude is suspicious, sullen, uncooperative, and dull. She speaks in a soft, reticent voice. After some questioning, she admitted that she was epileptic and had had many seizures until five years ago, when the use of phenobarbital was initiated. Since then her seizures, apparently grand mal, have been controlled. Typical responses follow: Jan. 6: "Any more questions? I'm out of answers." This she said irritably. She said the cotton test was "kid stuff."

Jan. 13: She was apathetic, dejected, discouraged.

Jan. 20: "I won't be much help today."

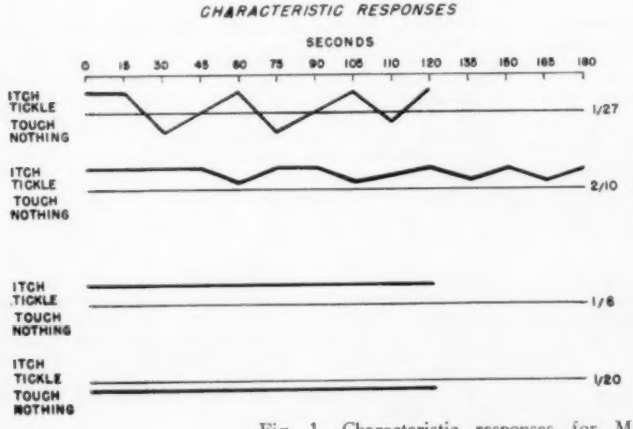
Feb. 24: She was huddled up, apathetic. She refused to cooperate for a self-administering Minnesota Multiphasic Test. Her attitude was suspicious. "Those questions have nothing to do with my skin."

Date	Patient's Reactions	Skin Responses
12/30/53	Uncontrollable itching complained of.	Seborrheic dermatitis, four months' duration, involving scalp, ears, forehead, axillae, pubic region, and vulva. Scalp: Thickened, crusted dermatitis. Forehead: Dermatitis is subacute; skin reddened and scaly. Pubic region: Acute, sharply marginated, erythematous, oozing, fissured dermatitis. Rt. forehead: Cotton stroking "soft" throughout, i. e., touch only. Central forehead: Skin normal except for a few papular lesions. Normal adaptation. Rt. antecubital fossa: Skin clear. Touch only. Rt. inguinal: Area of itchy dermatitis. No adaptation. Rt. upper thigh: Uninvolved skin, adjacent to an area of dermatitis. Shifting adaptation.
1/6/54	Irritable and uncooperative.	Eruption in groin a bit improved, but eruption is now present in new areas; e. g., blepharitis with edema, oozing, and crusting of the eyelids; more generalized erythema. Papular eruption of arms and forearms. Rt. forehead: Touch only. Rt. antecubital: A few papules and some excoriation. Touch only.

Date	Patient's Reactions	Skin Responses
		Rt. groin: Severe dermatitis. Itch only (one touch response in the test period). Lt. groin: No adaptation. Area of severe dermatitis.
1/13	More cooperative, apathetic, and dejected.	Dermatitis worse. Acute oozing of serum from ears. Rt. forehead: Dermatitis present. Touch only. Lt. upper lip: Normal adaptation. Rt. antecubital: Dermatitis present; shifting adaptation. Rt. groin: Severe dermatitis. No adaptation.
1/20	Mood apathetic.	Dermatitis of upper lids improved. Groin eruption involuting at periphery. New oozing areas in antecubitals, anterior neck, labia. Dermatitis of forehead worse. Rt. forehead: Touch only. Lt. upper lip: Normal adaptation. Rt. antecubital: Touch only. Rt. groin: Touch only. Lt. groin: Touch only.
1/27	Generally less itching; patient tired, but a bit brighter emotionally.	Pyoderma developed. Temperature 102 F. Penicillin given for this, and skin improved. Face, eyelids, ears improved. Skin dry and scaly. Acute oozing dermatitis of vulva and right antecubital fossa. Some eczematous reaction of legs. Rt. forehead: Touch only. Lt. upper lip: Touch only. Rt. antecubital: Shifting adaptation. Rt. groin: Touch only.
2/5	Mood apathetic.	Skin better. Practically no itching. Rt. forehead: Touch only. Lt. upper lip: Touch only. Rt. antecubital: Touch only. Rt. groin: Touch only.
2/10	Anxious; huddled up; apathetic.	Skin better. Skin of legs weeping. Rt. forehead: Touch only. Lt. upper lip: Touch only. Rt. antecubital: Touch only. Rt. groin: Touch only.

Total responses: Touch only 20. Normal adaptation 3. No adaptation 4. Shifting adaptation 3.

Comment.—The all-touch response is predominant in this patient. Few tendencies to adaptation were evident. As improvement in the dermatitis occurred, her responses became all-touch in areas which had previously showed no adaptation, i. e., had been all-itch. Her transference attitude was expressed in a wish to have minimum contact with us.



Upper graphs:
1/27: Left arm, area of excoriation.
2/10: Left forehead, area of dermatitis.
Lower graphs:
1/6: Left groin, area of severe dermatitis.
1/20: Left groin; area of involuting dermatitis.

Fig. 1.—Characteristic responses for Mr. B (upper graphs) and Mrs. A (lower graphs).

Seven months after our initial contact with this patient she was still hospitalized at Cook County Hospital for her dermatitis (Fig. 1).

CASE B.—Mr. B. is a 54-year-old bus driver. He is intelligent, frank, open, and cooperative. He readily admits he is emotionally labile, weeps and flushes easily, yet is able to exercise considerable superficial control. He complains of depressed feelings since his wife left him, five years ago, because of his reduced potency following a prostatectomy. Since then his mother has lived with him. He associates no specific events with the onset of his dermatitis three to four months before our first contact with him, at Cook County Hospital. He does believe the dermatitis is connected with nervousness. He cries and trembles easily. All this information came out very easily in a few minutes of conversation.

Date	Patient's Reactions	Skin Responses
1/6	Talkative; emotionally labile.	Diagnosis: Universal idiopathic exfoliative dermatitis, 3 months' duration. Myocardial infarction, 2 wks. Three months before a circumscribed patch of dermatitis had appeared in the sternal area. It did not respond to local or x-ray therapy and became generalized. At present the skin is exfoliating, thickened, lichenified; acute erosive crusting lesions on the dorsum of both feet. Patient now in hospital 6 wks. He says his initial severe itching is almost all gone. Lt. forehead: Shifting adaptation. Lt. nasolabial fold: Adaptation. Lt. antecubital: Adaptation. Lt. instep: Shifting adaptation.
1/13	His responses to stroking are strongly emotionally toned. Itch is felt very strongly. He gesticulates. Touch "feels good"; soothing. "I could go to sleep while you're doing that."	Dermatitis is unchanged. Exfoliate continues. Lt. forehead: Adaptation. Lt. nasolabial fold: No adaptation, but strong itch gradually moves in direction of tickle.
1/27	As always, outgoing and volatile! is irritable; complains of itching on arms.	Lt. antecubital: Shifting adaptation. Lt. forehead: Intense itching, followed by shifting adaptation. Lt. antecubital: Patient says this is the itchiest spot on his body. Shifting adaptation. His responses are either itch or that nothing is felt. Lt. arm, lateral aspect: Skin is excoriated here. Shifting adaptation.
2/3	On corticortropin for 5 days. Mood is not euphoric. He complains about the hospital food.	Striking improvement in skin. No exfoliation. Less lichenification. Lt. forehead: Adaptation. Initial responses of intense itch. Lt. antecubital: Adaptation. Lt. arm, lateral aspect: Adaptation.
2/10	Off corticortropin for 5 days. Skin much itchier. He is disgusted. Can't sleep. Given self-administering Minnesota Multiphasic. Very cooperative about filling it out and returns it promptly.	Lt. forehead: Area of dermatitis. Dry, scaly, thickened skin. No adaptation. Severe itch and tickle, with slight tendencies to shift from itch to tickle. Lt. Antecubital: Dry, scaly, thickened skin. Shifting adaptation. Lt. arm: Shifting adaptation.
2/17	Back on corticotropin b. i. d. Not much relief from it the second time. Patient is quite irritable.	Patient now complains of itching being replaced by burning on anterior chest, face, and arms. Skin in these areas is reddened. It looks like a burn. He has not had a dramatic corticotropin response this time. The eruption has not involuted as quickly, though there is some improvement. Lt. forehead: No adaptation. Response tends to go from itch to tickle. Lt. antecubital: Shifting adaptation. Lt. arm, lateral aspect: Shifting adaptation.

Total Responses: Shifting adaptation 10. Normal adaptation 6. No adaptation 3.

Comment.—This patient's marked emotional volatility, associated with some attempts at control, is exactly reflected in his predominant skin responses of shifting back and forth between erotism (itch and tickle) and control (shifting adaptation). The overcompensatory efforts at control result in frequent responses of minimal or absence of sensation, reported as "I feel nothing." All algedonic responses were very intense. When he does feel touch, he frequently describes it as "soothing." Thus, touch has for him its own pleasurable component (Fig. 1).

CASE C.—A 35-year-old white woman was studied as an inpatient at the Institute for Psychosomatic and Psychiatric Research, Michael Reese Hospital. Accordingly, considerable data are available, especially from the psychiatric side.

The patient was married six and a half years ago. Her neurodermatitis began less than four months after she was married. Prior to this there had been no skin disease, but she had suffered from "prickly heat" in the summers and had always had a delicate skin. Her dermatitis disappeared with her first pregnancy, four years ago, but it returned in localized form after her first child was born. With her second pregnancy, a couple of years later, the dermatitis became generalized. For a time it had been controlled by cortisone, but prior to her admission to the hospital this substance was no longer effective.

The patient's mother died in the flu epidemic of 1918, when the patient was six weeks old. She was the youngest of three children. The older children were placed in an orphanage. At the age of 6 months the patient was placed in a foster home. What happened to her between the age of 6 weeks and 6 months is unknown. She remained in this foster home until the age of 8 years. The foster father died when she was 2 years old, but she continued living with the foster mother. When she was 8, her father remarried and took her to live with him. She had received much attention from her foster mother, and this move made her unhappy. She came into a large poor family, with her own siblings and stepsiblings. Her father was grouchy and her stepmother chronically ill. She remained with them until she married, at 28.

She is a thin-lipped, overcontrolled woman. She resents her overdependent, hypercritical, hot-tempered husband, who embodies many of her own attitudes which are unacceptable to her. Her relation to her foster mother was one in which she received much attention but little physical contact, such as cuddling and kissing. She received little care of any sort after returning to her father and stepmother. At this time she cried a great deal, but gradually "overcame" her grief at leaving her foster mother. Since then she has cried little, and does not give in to her emotions. She says she holds too much feeling in. She does not enjoy physical contact with her husband or children. She feels close to no one. Embraces cause a hemmed-in feeling. She never asks her husband to scratch or rub her back to relieve her dermatitis. She is self-conscious about her skin trouble, having always felt that a clean and neat appearance was important. She is unable to relax. If she tries to, she still feels that she is working or running inside.

All sexual experiences have been unpleasant, and she avoids intercourse. She was unprepared for menstruation, which came as a shock, and she suffers from dysmenorrhea. After several interviews, considerable sexual curiosity and desire for sex information became apparent. Her extensive repression extends to her dream life. "I've not dreamed for years."

Typical nurses' notes describing her behavior in the hospital include "rather tense"; "remains in room much of time"; "generally seclusive of the group"; "pleasant but little socializing."

The initial formulation of this patient's emotional disturbance was as follows: overcontrolled neurodermatitis type. Superficial attitude is "touch me not," in reaction against strong unacknowledged dependent wishes. Physical contact is frightening. The attempted (manifest) functional level of autonomy and independence goes with an overt anal-dermal attitude—"the unclean, soiled skin." The latent dependent wishes are denied.

Date	Patient's Reactions	Skin Responses
5/8	Tense; appears overcontrolled.	Rt. forehead: (Skin reddened, thickened, dry, scaly, excoriated.) No adaptation. Itching throughout; occasional tickle or rub also felt.
		Rt. side of neck: (Dermatitis as above.) No adaptation. Itching throughout.
		Rt. antecubital: (Dermatitis as above.) No adaptation.

Date	Patient's Reactions	Skin Responses
5/12	More relaxed.	For past 36 hr. patient has been treating right side of forehead, face, neck, and right arm with 1% Neo-Cortef* ointment. Rt. forehead: (Dermatitis same on right and left.) Touch only. Rt. side of neck: (Dermatitis same on right and left.) No adaptation. Itch throughout, but it got milder toward end of test period, i. e., some tendency to adaptation. Rt. antecubital: No adaptation. More dermatitis on left (untreated) side than on right. No itching spontaneously on right. Itch spontaneously present on left. Lt. antecubital: No adaptation. Abdomen: (One inch to right of midline; no dermatitis in this area.) Touch only.
5/14	Some complaints about hospital noise; little change.	Skin better. Continuing Neo-Cortef on right side. Rt. forehead: (Eruption less. No spontaneous itch.) Touch only. Rt. antecubital: (Dermatitis much improved.) No adaptation. Abdomen: (Area of normal skin.) Adaptation.
5/17	Little change.	Rt. antecubital: (Skin paling. Still lichenified.) No adaptation. Abdomen: (Area of normal skin.) Touch only. Rt. anterior thigh: (Normal skin, cf. her frigidity.) "Do not feel anything."
5/19	Patient opens up a bit on sexual topics. Generally little change.	Skin generally better. Less redness. Rt. forehead: No adaptation. Rt. antecubital: No adaptation. Rt. side of neck: Shifting adaptation. Rt. abdomen: Touch only. Rt. anterior thigh: Adaptation.

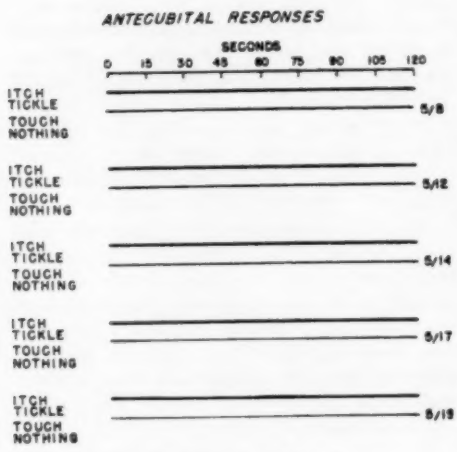


Fig. 2.—Antecubital responses, Mrs. C.
5/8: Skin reddened, scaly, excoriated.
5/12: On 1% hydrocortisone ointment for 36 hours, dermatitis somewhat improved.
5/14: Continuing on hydrocortisone ointment, dermatitis vastly improved.
5/17: Skin still improving, but lichenified.
5/19: Improvement continues. No hydrocortisone for 36 hours.
NOTE:—Despite medication and skin improvement, the response continues as unchanged itch.

Total responses: Touch only 5. Normal adaptation 2. No adaptation 10. Shifting adaptation 1. (Fig. 2).

Comment.—It is striking that in this patient there were only two responses of normal adaptation. Either the responses were exclusively algedonic (of the pleasure-pain series), and the quality of the algedonic responses was exclusively that of itch, the more pleasurable tickling not being reported, or they were exclusively responses of touching or rubbing.

This finding corresponds very closely to the patient's manifest transference responses and to her reactions to life situations. Either she permits limited utilitarian contact, without any of the algedonic pain-pleasure quality, or she experiences sensual contact exclusively in terms of the painful (itching) end of the pleasure-pain spectrum.

* An ointment containing hydrocortisone acetate in 1% or 2.5% concentration and neomycin sulfate 0.5%.

On discharge from the hospital, though her dermatitis was much better, it was clear she had achieved no resolution of her intrapsychic and interpersonal difficulties. Her dermatitis soon flared up again, and she entered psychotherapy. After four months of psychotherapy her dermatitis is still present.

CASE D.—D, a 39-year-old business man, was also studied and treated at the Institute for Psychosomatic and Psychiatric Research and Training of Michael Reese Hospital. A large, active man, outgoing and friendly, he is married and has three children. At the age of 14 a neurodermatitis began to develop on the flexor aspects of his arms and legs, spreading to involve his buttocks, genitals, and abdomen. These episodes of dermatitis would come on only after swimming and would subside in a few days. He enjoyed swimming greatly, but could feel the dermatitis coming on while he was in the water. In August, 1953, after going swimming twice, he developed edema of the eyelids. He was treated by one of us (M. R.) with cortisone ointment, to which he responded well. Later a large patch of dermatitis developed on his left arm and gradually spread. Six weeks before his hospitalization he stopped working because of severe pruritus and insomnia. The onset of dermatitis in the summer of 1953 was associated with his concern about his wife's anxiety over her mother's illness. This was a threat to his own dependent needs. He was also in conflict with his wife, who insisted he take a vacation. He felt he had to stay on the job and visited her and his children only weekends. It was while swimming on these weekends that the current exacerbation began. Since that time he has been troubled by business conditions and difficulties with his children. He finds the severe pruritus both disturbing and erotically gratifying.

There is a considerable family history of allergies. His father is a gentle, passive introverted man. His mother is affectionate, motherly, and aggressive; a "doer." The patient has two older sisters. D is aware that he has always been in conflict over his attachments to his father and his mother. He has always been active and hard-working, never a fighter. His interests are in engineering, but he has become involved in sales because of his gregariousness. He began suffering with abdominal pains at 21, and at 23 had a gastroenterostomy for peptic ulcer.

Typical nurses' notes: "Patient is extremely pleasant and friendly. Takes paternal role on the unit." "Friendly and pleasant as usual. Said, 'It's wonderful what a rest will do.' Socialized well with the group."

Date	Patient's Reactions	Skin Responses
3/3	Some pressure of speech. Talks freely about some guilt feelings from early adolescence.	Generalized neurodermatitis. Dermatitis is present in patches on ears, shoulder, neck, thighs, chest, and abdomen. Areas of normal skin intervene between areas of dermatitis. Lt. forehead: (Skin clear.) Adaptation. Lt. anterior shoulder: (Skin reddened, scaly, subacute dermatitis.) No adaptation. Lt. antecubital: (Minimal dermatitis.) Adaptation. Rt. anterior thigh: (Subacute dermatitis.) No adaptation Rt. anterior thigh: (At periphery of area of dermatitis. No dermatitis here but skin is slightly reddened.) Shifting adaptation.
3/5	His self-driving tendencies discussed. Less tense than on 3/3.	Skin improved. Lt. forehead: (Skin clear.) Adaptation. Lt. antecubital: (Dermatitis present.) No adaptation. Rt. anterior thigh: (Less dermatitis.) No adaptation, but early signs of partial adaptation; i. e., feels tickle and rub simultaneously.
3/8	Tension at about level of 3/5. His perfectionism discussed. Becomes somewhat aroused and itchy as he discusses pressure of his job; his desire for his sons to be perfect; his resentment of any setback.	Skin much better. Lt. forehead: (Skin clear.) Adaptation. Lt. antecubital: (Dermatitis much better.) No adaptation. Rt. thigh: (Dermatitis improved.) No adaptation but tendencies to partial adaptation; i. e., tickle and rub are felt simultaneously. Rt. thigh: (Adjacent to area of dermatitis. Skin slightly reddened.) No adaptation.
3/10	Improving slowly. Considerable conscious con-	Skin much better. Little scratching. Less sedation needed at night.

Date	Patient's Reactions	Skin Responses
	trol of inner feelings of insecurity. His self-demands are because of his fears of deprivation. The higher he goes, the more he fears falling. The necessity of accepting his dependent needs was discussed.	Lt. forehead: (Skin clear.) Adaptation. Lt. antecubital: (Dermatitis disappearing.) No adaptation, but tendencies to partial adaptation; i. e., occasionally rub is felt along with tickle. Rt. thigh: (Dermatitis involuting. Skin smooth, thin, erythematous. No scaling or crusting.) Partial adaptation. Rt. thigh: (Adjacent to area of dermatitis.) Partial adaptation.
3/13	Much more relaxed. Able to sleep through the night. His need to surpass his father and his feeling he couldn't depend on his father discussed.	(Skin tests of 3/12.) Skin much better; Still pinkish red. Itching minimal. He can now rub skin without intense erotic pleasure, indicating the absence of "itchy skin." Lt. forehead: Adaptation. Lt. antecubital: Partial adaptation Rt. thigh: Adaptation (first time). Rt. thigh: (Adjacent to area of dermatitis.) Adaptation (first time).
3/15	Relaxed. Some anxiety about how he'll get along when he goes home. No new material elicited. He is ordering his defenses prior to leaving the hospital.	Skin clear. No eruption. Occasionally a slight itching on sides of neck and left antecubital. Skin does not tingle on excitement. No more desire to tear into self and scratch all over. Lt. forehead: Adaptation. Lt. antecubital: Adaptation. Rt. thigh: Adaptation. Rt. thigh: (Adjacent to former area of dermatitis.) Adaptation.
3/17	Relaxed. Sleeping without sedation. Desirous of leaving hospital, though not pressing.	No dermatitis. Occasional itch in left antecubital area. No sedation in past two days. *Note by Dr. Townsend Friedman:* Skin reaction to allergens was strongly positive on 2/2, 2/4, and 2/9. Now, on retesting, it is much diminished. Lt. forehead: Adaptation. Lt. antecubital: Adaptation. Rt. Thigh: Adaptation. Rt. Thigh: (Adjacent to former area of dermatitis.) Adaptation.

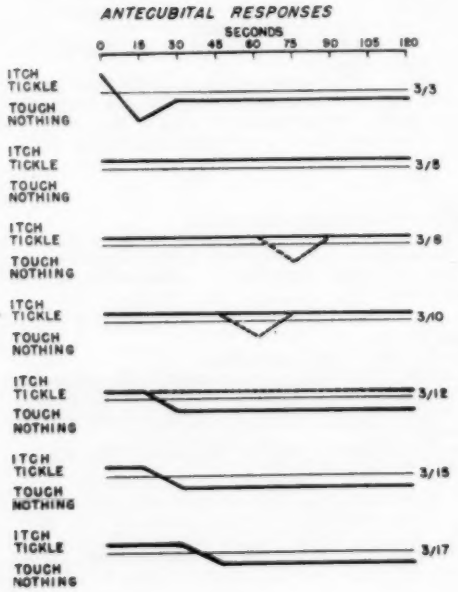


Fig. 3.—Antecubital responses for Mr. D.
3/3: Slight amount of dermatitis.
3/5: Dermatitis present, scratch marks.
3/8: Dermatitis improved.
3/10: Dermatitis disappearing.
3/12: Dermatitis almost gone.
3/15: Dermatitis is gone.
3/17: Dermatitis is gone.

Total Skin Responses: Normal adaptation 16. No adaptation 8. Shifting adaptation 1. Partial adaptation 3 (Fig. 3).

Comment.—This patient, even at the height of his neurodermatitis, had areas of normal adaptation. His social and vocational life has been relatively successful. He is outgoing, friendly, and warm. He readily accepts insight into and gratification of his dependent needs. In areas where there was no adaptation his skin responses were mainly of tickle. This indicates that within the pleasure-pain series, his responses tend toward the pleasurable end of the spectrum. These responses of no adaptation moved in the direction of normal adaptation, accompanying clinical improvement of the skin. The change from no adaptation to normal adaptation lagged about a week behind the clinical dermatological improvement. This patient left the hospital improved both dermatologically and in his general outlook. His skin has remained relatively well over a four-month period (to date), without any further psychotherapy.

CASE E.—E, a single woman of 53, was also studied at Michael Reese Hospital. She is a childish person, naïvely pseudoseductive, full of tears, which overflow without restraint whenever she is granted a sympathetic ear. She had lived with her mother until the latter's death from carcinoma, two years ago, after four years of complete invalidism. After her mother's death, she began to weep a great deal, bemoaning her own wasted years. She also felt she had changed from her happy-go-lucky personality into a nag like her mother. She noted increasing difficulty in supervising the women who worked under her in her capacity of office manager. A year ago she was hospitalized for a folliculitis of the external genitalia. While in the hospital, she was reprimanded by a nurse and soon afterward her "privates began to weep." A neurodermatitis developed and spread to her face, neck, and arms. She improved and returned to work, where she noticed her boss now seemed to prefer a younger girl to her, whereas previously she had been his confidante. She became jealous, and her dermatitis grew worse. She has been menopausal for the past 18 months, and has been somewhat depressed, with occasional suicidal thoughts.

She is the oldest of three children, having two younger brothers. She was devoted to her father, a traveling man, home only on weekends. Her mother was nagging, punitive, suspicious. She continually accused the father of infidelity and was jealous of the patient's attachment to her "daddy," who gave her everything she wanted. She married a young man when she was 19 and was divorced five years later. Her father died eights years before. During her mother's terminal illness she rarely went out for fear her mother would fall from her wheel chair and be killed. Once she did go out during this time to receive a bowling trophy. She felt her face and neck flushing, and the following day a dermatitis appeared, which disappeared after several months of dermatologic therapy.

This woman has never been able to express anger. She had a typical hostile-dependent relationship to her mother, frequently seen in women with neurodermatitis. She is a characteristic labile neurodermatitis type,† overflowing with tears, who tells her whole life story in five minutes. Strong childish dependent needs for close physical contact are at the surface of her personality.

Typical nurses' descriptions of her behavior follow: "She enjoys her stay here. She remains in bed much of the time. She is often seen examining her body and face. Appears tense and quite flghtly. Complaints are poutingly verbalized." "Alternates between seclusiveness and sociability."

This patient's skin reactions were tested by one of us (M. R.) and by a woman nurse on alternating days to see whether there was any difference in her responses to the examiners of a different sex.

Date	Patient's Reactions	Skin Responses
11/12	Second hospital day. Tearful, cried within 1 min. of beginning interview.	Neurodermatitis of face, neck, scalp, ears, anterior chest, antecubital fossae (tests by M. R.). Rt. forehead: (Skin reddened, thickened, scaly.) No adaptation. Tickle throughout. Rt. antecubital: (Dermatitis present, but less than on forehead.) No adaptation. Tickle throughout. A couple of tickle-rub responses. Rt. thigh: (Anterior surface.) No dermatitis. Touch only.

† References 11 and 15.

Date	Patient's Reactions	Skin Responses
11/15	More control. Did not weep until interview had lasted 5 min. Upset about losing her boss' interest.	Skin is better. On Neo-Cortef on left side, petrolatum (Vaseline) on right. She thinks there is less itching on Cortef side. Left antecubital fossa is less inflamed than right (tests by M. R.). Lt. forehead: No adaptation. Tickle and a few tickle-rub responses. Rt. forehead: Same responses as left. Rt. antecubital: No adaptation. Tickle only. Lt. antecubital: Touch throughout.
11/16		Tests by nurse. Lt. forehead: No adaptation. Tickle throughout. Occasional rub responses indicating tendency to shifting adaptation. Rt. forehead: No adaptation. Same as left. Rt. antecubital: Reversed reaction-rubbing, followed after 30 sec. by tickle only. Lt. antecubital: No adaptation. Tickle only.
11/17	Better spirits. Eyes fill with tears several times during interview, but she does not weep. Discusses some sexual problems.	Tests by M. R. Skin better. Lt. forehead: Less redness than on right. No adaptation. Rt. forehead: No adaptation. Rt. antecubital: (Edema of skin nearly gone. No scaling, slightly reddened.) No adaptation. Lt. antecubital: No adaptation.
11/18		Tests by nurse. Lt. forehead: No adaptation. Rt. forehead: No adaptation. Rt. antecubital: No adaptation. Lt. antecubital: No adaptation.
11/19		Tests by M. R. Lt. forehead: (Dermatitis worse. Skin reddened, edematous, scratched.) No adaptation. Rt. forehead: (Dermatitis same as on left.) No adaptation. Rt. antecubital: (Dermatitis worse.) No adaptation. Lt. antecubital: (Dermatitis better in this area.) Adaptation.
11/20	Skin became worse two days ago. Worried about returning to work. Feels she can't cope with job problems. Very tearful, like a helpless child.	Tests by nurse. Lt. forehead: No adaptation. Rt. forehead: No adaptation. Rt. antecubital: No adaptation. Lt. antecubital: No adaptation.
11/21		Tests by nurse. Results identical with those of preceding day, 11/20.
11/22	Upset. Itchy. Weeps throughout interview. Frightened that on leaving hospital in next day or two she'll lose her job. No attempts at reassurance.	Skin improved over 11/19. Both sides equally improved. Tests by M. R. Rt. forehead: No adaptation. Rt. antecubital: No adaptation. Lt. forehead: Slow adaptation. Lt. antecubital: No adaptation.
11/22	Reinterviewed. Much support and encouragement by therapist. She was diverted from weeping and left interview superficially cheered.	Given emotional support by M. R. during testing. Rt. forehead: No adaptation. Lt. forehead: Partial adaptation. Lt. antecubital: Shifting adaptation. Rt. antecubital: Not tested.

Total Responses: Touch only 2. Normal adaptation 2. No adaptation 27. Shifting adaptation 1. Partial adaptation 1. (Fig. 4).

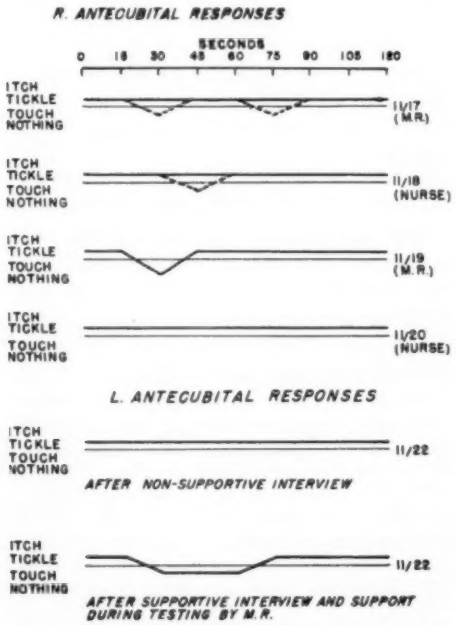


Fig. 4.—Antecubital responses (Miss E), tested on alternate days by Dr. Robin (M. R.) and by a female nurse.
11/17: Skin slightly reddened; little edema, no scaling.
11/19: Dermatitis worse.
11/22: Patient wept throughout nonsupportive interview, of 15 minutes; reinterviewed and given encouragement, diverted from weeping.

Comment.—This woman, a typical overflowing neurodermatitis patient, in the main showed responses of no adaptation, which consisted of tickle, thus being at the pleasurable end of the pain-pleasure spectrum. There did not appear to be any significantly different responses to testing by the physician and by the nurse. Positive emotional support seemed to shift her responses in the direction of adaptation. She has responded well to superficial, supportive outpatient therapy.

Comment

Our test of skin sensations is, in effect, a measure of what might be called transference attitudes, functioning at a relatively simple level. Grace and Graham [8] consider that specific attitudes toward certain situations are accompanied by certain specific bodily changes which may lead to pathology. They state:

> The reaction of an adult human being consists of an *attitude*, which can be expressed verbally, and accompanying *bodily changes*. By "attitude" is meant the way in which he perceives his own position in the situation, and the action, if any, which he wishes to take to deal with it.

We use the term transference attitude in this way and find that its variations in a particular experimental situation are reflected in the varieties of sensory response we are describing. Though we do not place our emphasis on the subject's conscious awareness of his attitudes, we do find that what is related to our sensory experiments is not deeply buried unconscious mental content, but manifest content, as exemplified in words and behavior. Transference attitudes, as measured here, really reflect the subject's attitude, expectations, and feelings about a particular sample of contact with the external world, the stroking of his skin with cotton wool by the physician in the experimental situation. As one might expect, these skin sensations correspond quite closely to certain general or total reactions of the subjects.

If we compare Mrs. C and Mr. D, for example, we find the following:

Transference Attitudes

Mrs. C

Over controlled, thin-lipped. Superficial attitude is "touch-me-not." Sensual pleasure is unacceptable. Physical contact is frightening. Her attitude toward her physicians is hostile, cool, aloof, and somewhat suspicious. Her dependent needs are thinly concealed.

Mr. D

Pleasant, friendly, outgoing, warm. His attitude toward his physicians is one of accepting insight. He readily accepts gratification of his dependent needs. He obtained considerable sensual pleasure from scratching.

Skin Responses

Only two responses of normal adaptation. All the responses in the pain spectrum were of itching. She felt no tickle, or responses were exclusively of touch. Even with clinical improvement, her sensory responses remained unchanged.

Areas of normal adaptation existed even at the height of his dermatitis. In areas of no adaptation

his responses were mainly of tickle (in which there is more pleasure and less destruction than in itch), and they became more normal adaptation responses as the skin improved, lagging about one week behind the skin improvement.

I. Phylogenetic and Biological Implications

Phylogenetically, pain is the most primitive sensation. Anatomically, it is carried by unmyelinated or fine myelinated fibers. Touch is phylogenetically of more recent origin and is transmitted by large myelinated fibers. Touch seems to have an inhibitory effect on pain. In its absence pain perception becomes more primitive and intense (protopathic). Here, as in other functions of the nervous system, the later-acquired systems have a certain inhibitory effect on those of earlier origin. Zotterman [18] points out that tickling is easily stopped by rubbing the skin, and that firm pressure on the skin does not cause tickle, both instances of inhibition by touch of a sensation belonging to the pain series. He concludes: "Fast impulses traveling up the posterior columns inhibit the central effect of the later arriving slow impulses. The less the large, fast fibers are stimulated the more intense become the tickling and itching sensations elicited by the slow impulses." He quotes O. Foerster to the effect that dorsal-column lesions in the cord lead to a hyperalgesia "due to an exclusion of the highly differentiated and phylogenetically younger system of cutaneous sensory fibers, which normally exert an inhibitory influence upon the very ancient system of pain fibers."

Ordinarily, it is a characteristic of touch that it adapts rapidly, whereas pain adaptation is very slow. Our technique involves the use of repetitive stimuli with cotton. That touch ordinarily does not adapt under these conditions is explicable as due to the repetitive stimulation of the tactile receptors. That tickle (a member of the pain series) ordinarily does adapt readily, though there is no adaptation to repetitive pain stimuli, e. g., pinpricks, is of some interest, especially as there is less tendency to adaptation when the response to the cotton stroking is described as itching (i. e., closer to pain) than when it is described as tickle. Perhaps, as a result of some central neurophysiological process, when peripheral stimulation of the pain system moves in the direction of the pleasure end of the pain-pleasure spectrum, i. e., toward tickle, it may be more subject to regulation by the phylogenetically newer touch systems than are pain sensations.‡

II. Relationship to Psychological Structures

The pain-pleasure spectrum of the pain system is closely related to erotic instinctual life, in its pleasurable and painful aspects. This has been referred to by many authors, for instance, by Dunbar,[2] who attributes the following statement to Sadger:[3]

> The most intimate connection with the sexual life is seen in that modification of skin sensibility which we call tickling. One evidence, among others, of the sexual nature of this sensation is seen in the fact that many languages have only one word for tickle and cohabit. Many extremely ticklish girls cease to be ticklish as soon as they begin regular sexual intercourse, and in many folk traditions ticklishness serves as proof of sexual integrity.

The touch system is more closely related to those exteroceptive functions of discrimination and reality testing which are part of ego functioning. The course of sensory evolution could be considered as an attempt to develop finer discrimination in order to avoid excessive stimulation of the primitive, diffuse, pain-withdrawal system. The touch system thus contributes to the protection against excessive stimuli (*Reizschutz*), for it enables the individual to avoid pain. For instance, one can *touch* the point of a pin, recognize it and, hence

‡ Is tickle an evidence of a phylogenetic trend toward a sort of "civilizing" or drawing the teeth of the pain system? Tickle is related to laughter, wit, and humor. The relationship between pain and tickle and psychic pain and humor may be only analogic, but it is of interest to consider Freud's[6] suggestions that the humorist deals with psychic pain on the model of the grown-up laughing at his childish sorrows. His grown-up ego is too big to suffer under circumstances which would be intensely painful to his infantile ego. Here, what was once pain becomes humor, though the pain is immanent in the humor.

avoid pricking pain, which would result from firm pressure instead of touch. It would be more accurate to state that the pinprick is felt as sharp and as something to be avoided because of the admixture of a minimal amount of pain with the touch discrimination. This corresponds exactly to the use of anxiety as a signal by the ego.

The sense of touch may be regarded as one of those "ego-apparatuses" described by Hartmann.[9] He points out that certain somatic and psychic functions of the organism, from the time of differentiation of the ego and the id, are in the service of the ego. Though they may become involved in psychic conflicts, their contribution is essential to the formation of the so-called autonomous, or conflict-free, area of the ego. Touch, being further from instinctual life, and basically exteroceptive, is much more closely linked to the ego than is the pain system. It has to do with reality testing and the filtering out of excessive stimulation. It is, therefore, fundamental to the development of mature object relationships. Excessive perception of stimulation leads to excessive response. The ego may exercise control of both stimulus and response.

III. Significance of Types of Response in Total Personality Functioning

The principal types of response to cotton-wool stroking that we have observed have been described above. What is their significance in terms of the whole person, of which they are but one small facet?

A. "Normal" adaptation. This we assume to represent an optimum level of integration of instinctual life and ego functioning, as reflected in skin sensation. We chose this as our norm, not on a statistical basis, but on the basis of our experiments, using ourselves as subjects,[12] and on the basis of our theoretical preconceptions which were reinforced by clinical experience. We consider that in the adult the experience of being stroked with cotton is ordinarily first felt as tickle, but then is quickly (usually within 30 seconds) replaced by sensations of touch or rubbing. This may be interpreted as follows:

1. The capacity for experiencing sensual pleasure, mediated by the pleasure-pain system, is present, but the ego, while permitting this pleasure, retains control and does not permit itself to be overwhelmed by sensual stimulation (e. g., tickle) or by more painful experience, such as itch.

2. The erotic transference reactions of the subject to the experimenter, while present, are not permitted to get out of control, but, instead, are soon replaced by the more reality-oriented touch sensations.

B. No adaptation. Responses are entirely algedonic, i. e., of the pleasure-pain series. Here the ego does not have the capacity to control instinctual reactions §; the erotic transference is unchecked. It may be mainly pleasurable, or it may be masochistic, as more painful elements, such as itch, are brought in.

C. Touch throughout. The capacity of experiencing sensual pleasure has been repressed. The affective aspects of the transference reaction are absent.

D. Shifting adaptation. This indicates an active, unsettled struggle between instinctual forces and the ego's attempts to control them.

E. Partial adaptation. This is close to normal adaptation, but with a somewhat lower degree of ego control operating. It is a transitional state.

IV. Personality Types Associated with Differing Types of Skin Response

Here we come to more speculative ground. We are also faced with a question: Though there is a relationship between these skin responses and certain personality types (or characteristic modes of reaction, or typical defensive patterns), of what does this relationship consist?

It would be misleading to say that "nor-

§ The ego function influencing control is the capacity for delay or inhibition of immediate discharge of feelings to the outside. Here is a simple instance of ego control over affects, and of ego function in delimiting the person from his milieu. It has been noted[10] that movement of feeling to the surface is frequently associated with the development of symptoms on the body surface.

mal" adaptation occurs in "normal" persons. After all, it is a peripheral response, and as such cannot reflect the nuances of personality. It does occur in subjects in whom marked evidences of psychopathology were not superficially evident, in a few moments of conversation. It occurs in persons whose transference responses on immediate contact were not marked either by excessive "overflowing" emotionality or by excessive coldness and rigidity. Obviously, within this broad area much psychopathology may exist, which is not instantly apparent; e. g., we have observed "normal" adaptation in a frankly paranoid patient, who, however, related in a friendly and open way to the examiners.

The absence of adaptation is usually associated with responses in other areas of skin of the same subject which are exclusively of touch. The middle ground of "normal" adaptation is not prominent. These are people whose defenses are rigid. They defend themselves against flooding with uncontrollable instinctual impulses by attempts at complete repression of affect. The ego and the id are so at war with each other that, at least as shown in their dermal responses, coexistence is difficcult. One or the other preempts the sensorium. Patients whose interpersonal relationships are polar, either intensely erotized or cool and aloof, reflect this same dichotomy on the transference level. Clinically, adults who tend to enjoy only fantasy, (especially of a sadomasochistic character, related to the pain-pleasure system) and who find reality barren and uninteresting (touch alone; no sensuality) correspond to these subjects who only feel either tickle or itch exclusively, or touch exclusively, and never experience the interrelationship of the two which is demonstrated in "normal" adaptation.

It appears reasonable to relate these concepts to observations made by others in somewhat different, but related, spheres. Frenkel-Brunswik [7] started from the problem of personality and ethnic prejudice and then attempted to demonstrate that in more or less emotionally neutral perception experiments the personality factors underlying ethnic prejudice would also be apparent. She points out that it is the rigid, prejudiced, authoritarian personality who also perceives in terms of extreme opposites, (e. g., either extreme abstractness or extreme concreteness), and is strongly stimulus-bound, and is intolerant of perceptual ambiguity. She concludes:

> In general, severe repression of certain tendencies such as aggression toward authority, fear, weakness, or elements of the opposite sex in oneself, find their parallel in an externalized image of these tendencies as projected onto others and in a narrowness and rigidity of consciousness. There is more than an empirical affinity between the strength of hostility, of power-orientation, of externalization, and of rigid stereotyping, on the one hand, and the intolerance of ambiguity on the other; there is a similar affinity between the orientation toward love and the acceptance of drive impulses, on the one hand, and a general flexibility, on the other. The struggle between these two orientations is basic to our civilization; its individual members display these two patterns in varying proportions and changing configurations.

Margolin [14] psychoanalyzed a woman with a gastric fistula, whose gastric functioning was independently studied by gastric physiologists. Her gastric activity was found to occur in three patterns: synchronized high activity; synchronized low activity, and dissociation or asynchrony of the gastric functions tested, which were total secretion, acidity, pepsin, blood flow, and motility. He found:

> When the repressed instinctual need mobilized by a stimulus in the experimental situation is about to emerge into consciousness, the gastric functions are in a state of associated high activity. Should reaction-formation become the dominant defense . . . the pattern is one of associated low activity. If the defense mechanisms succeed in establishing psychic equilibrium, then the pattern of random fluctuation or, in the language of general physiology, dissociation is manifested.

The pattern of high gastric activity and emerging of repressed instinctual need parallels our formulation of no adaptation responses. The pattern of low gastric activity and reaction formation parallels our formulation of touch-only responses. Per-

haps asynchrony of gastric function, tolerance of perceptual ambiguity, and a cutaneous response of normal adaptation are all manifestations, at different levels, of the same basic aspects of personality.

This raises certain interesting questions regarding the relative stimulation of the pain and touch systems of the infant by its mother. Spitz [17] and Rosenthal [16] have discussed the role of maternal handling or its lack in the genesis of infantile eczema. We might speculate as to what in the child-mother relation would tend to produce a fixation on the touch or on the pleasure-pain system of the skin. If there is something about the child which pains the mother, will she in some way respond to stimulate its pain system? Touch may be a source of gratification too. Is some of the capacity for tactile pleasure made possible by the mother's tender handling of the child? And could this pleasure serve partly to neutralize the more primitive, and sometimes masochistic, pleasure of the pain system? || Touch may be enjoyed and described as soothing, but this touch pleasure does not appear to exist if algedonic pleasure is completely repressed. When touch is used like a defense against algedonic pleasure, it is not pleasurable itself. This is comparable to the fact that if the ego is engaged in an all-out battle with instinctual forces, the ego's own functioning is not the source of pleasure and well-being that it may be under less conflictual circumstances. In a sense, the dichotomy between the pain-pleasure system and the touch system corresponds to the dichotomy between the pleasure principle and the reality principle. It is striking that the interrelationship of the two sensory systems, pain and touch, exemplifies, in a simple way, many of the higher levels of psychological functioning. We must wonder whether similar interrelationships could be observed in organs other than the skin, and whether disturbances in these interrelationships are also associated with dysfunction and disease.

|| Rosenthal believes infantile eczema originates in the "lack of soothing skin experiences in these infants. Their mothers tend to avoid physical contacts with them. For such infants there would be inadequate counterbalancing of unpleasant skin experiences with pleasant ones."

Summary and Conclusion

When the skin is lightly stroked with cotton wool for a two-minute test period, several types of subjective responses appear. These are as follows:

(*a*) Normal adaptation, in which sometime within the test period an initial sensation of itch or tickle is replaced by touch

(*b*) No adaptation, in which tickle or itch only are perceived during the test period

(*c*) Touch throughout

(*d*) Shifting adaptation, in which responses tend to alternate between tickle and touch

(*e*) Partial adaptation, in which there is a dimunition, but not complete disappearance, of itch or tickle sensations during the test period

A pilot study of a number of patients with various dermatoses indicated that emotionally labile patients tended to show no adaptation, whereas more controlled persons showed normal adaptation.

Five patients with various dermatoses were studied while hospitalized, and their reactions to cotton stroking were compared with their personality structures, transference attitudes, and state of the dermatoses. Some of our observations on these patients follow: Those whose transference responses tended to be of the all-or-nothing type, i. e., either excessively defensive or excessively, ill-controlledly emotional, generally showed all-or-nothing skin responses—either all itch-tickle or all touch. As their dermatoses improved, the all-itch responses became touch-only responses. Patients whose affects were better integrated and less polar showed more skin responses of normal adaptation. As their dermatoses improved, tickle-only responses changed to normal

adaptation. A patient showing marked emotional volatility, with some attempts at control, vacillated between itch-tickle and touch sensations, exhibiting shifting adaptation.

By and large, the severer the emotional constriction and the more intrapunitive the patient, the more responses of itch rather than of tickle were elicited. This seems to be connected with the fact that itch is closer to the pain end of the pleasure-pain spectrum than is tickle.

The pain-pleasure series (pain, itch, tickle) is closely related to erotic instinctual life. The touch system is related to and subserves ego functioning. Responses of normal adaptation appear related to optimum balance between erotic, instinctual life, and ego control, insofar as this can be reflected in the skin. Reactions of no adaptation (all itch or tickle) indicates excessive emotionality and deficient control. Touch-only reactions are correlated with attempts at excessive and rigid control or affects.

109 N. Wabash Ave.
116 S. Michigan Ave.

REFERENCES

1. Blake, R. R., and Ramsey, G. V.: Perception: An Approach to Personality, New York, The Ronald Press Company, 1951.

2. Dunbar, H. F.: Emotions and Bodily Changes, New York, Columbia University Press, 1935.

3. Sadger, J.: Haut-, Schleimhaut- und Muskelerotik, Jahrb. psychoanalyt. u. psychopath. Forsch. 3:525-556, 1912.

4. Freud, S.: The Ego and the Id, London, Hogarth Press, Ltd., 1949.

5. Freud, S.: Three Essays on the Theory of Sexuality, London, Imago Publishing Company, Ltd., 1949.

6. Freud, S.: Wit and Its Relation to the Unconscious, New York, Dodd, Mead & Company, Inc., no date.

7. Frenkel-Brunswik, E.: Intolerance of Ambiguity as an Emotional and Perceptual Personality Variable, J. Person. 18:108-143, 1949.

8. Grace, W. J., and Graham, D. T.: Relationship of Specific Attitudes and Emotions to Certain Bodily Diseases, Psychosom. Med. 14:243-51, 1952.

9. Hartman, H.: Ego Psychology and the Problem of Adaptation, in Organization and Pathology of Thought, David Rapaport, Editor, New York, Columbia University Press, 1951.

10. Kepecs, J. G.: Some Patterns of Somatic Displacement, Psychom. Med. 15:425-432, 1953.

11. Kepecs, J. G.: Rabin, A., and Robin, M.: Atopic Dermatitis: A Clinical Psychiatric Study, Psychosom. Med. 13:1-9, 1951.

12. Kepecs, J. G., and Robin, M.: Studies in Itching: I. Contributions to an Understanding of the Physiology of Masochism, Psychosom. Med. 17:87-95, 1955.

13. Klein, G. S., and Schlesinger, H.: Where Is the Perceiver in Perceptual Theory, J. Person. 18:32-47, 1949.

14. Margolin, S. G.: The Behavior of the Stomach During Psychoanalysis, Psychoanalyt. Quart. 20:349-373, 1951.

15. Rabin, A., and Kepecs, J. G.: Personality Structure in Atopic Dermatitis: A Rorschach Study, J. Gen. Psychol. 50:171-80, 1954.

16. Rosenthal, M. J.: Neuropsychiatric Aspects of Infantile Eczema, A. M. A. Arch. Neurol. & Psychiat. 70:428-451, 1953.

17. Spitz, R.: The Psychogenic Diseases of Infancy: An Attempt at Their Etiologic Classification, in Psychoanalytic Study of the Child, edited by Ruth S. Eissrer, and others, New York, International Universities Press, 1953, Vol. 6, p. 255.

18. Zotterman, Y.: Touch, Pain and Tickling: An Electrophysiological Investigation on Cutaneous Sensory Nerves, J. Physiol. 95:1-28, 1939.

Books

BOOKS RECEIVED

We acknowledge receipt of the following books. Only those books will be reviewed which the Editorial Board finds suitable for this journal.

Patterns of Mothering: Maternal Influence During Infancy. By Sylvia Brody, Ph.D. Price, $7.50. Pp. 446. International Universities Press, Inc., 227 W. 13 St., New York 11, 1956.

The Mentally Retarded Patient. By Harold Michal-Smith, Ph.D. Price, $4.00. Pp. 203. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5, 1956.

Experiencing the Patient's Day: A Manual for Psychiatric Hospital Personnel. By Robert W. Hyde, M.D. Price, $2.20. Pp. 214. G. P. Putnam's Sons, 2 W. 45th St., New York 16, 1955.

Transvestism. Edited by David O. Cauldwell, Sc.D., M.D. Price, $3.00. Pp. 128. Sexology Corporation, 154 W. 14th St., New York 11, 1956.

The Psycho-Medical Guide. By Curt S. Wachtel, M.D. Price, $5.00. Pp. 318. The Psycho-Medical Library, Inc., Tribune Building, 154 Nassau St., New York 38, 1956.

A Follow-Up Study of War Neuroses. By Norman Q. Brill, M.D., and Gilbert W. Beebe, Ph.D. Price not given. Pp. 393, with 271 tables and 11 figures. U. S. Government Printing Office, 1956.

The Sexual Responsibility of Woman. By Maxine Davis. Price, $4.00. Pp. 299. The Dial Press, Inc., 461 Fourth Ave., New York 16, 1956.

Modern Hypnotism: Key to the Mind. By. S. J. Van Pelt, M.B., B.S. Price, clothbound, $2.50; soft bound, $1.00. Pp. 88. Associated Booksellers, 2106 Post Rd., Westport, Conn., 1956.

Medizinische Psychologie. By Ernst Kretschmer. Price, $7.05. Pp. 382. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N. (American Zone) (agents in the U.S.A. and Canada, Intercontinental Medical Book Corporation, 381 4th Ave., New York 16), 1956.

The Nurse and the Mental Patient: A Study in Interpersonal Relations. By Morris S. Schwartz, Ph.D., and Emmy Lanning Shockley, R.N. Price, $3.50. Pp. 289. Russell Sage Foundation, 505 Park Ave., New York 22, 1956.

Dessins et peintures des alienes. By Irene Jakab. Price not given. Pp. 148, with 131 illustrations. Maison d'Edition de L'Academie des Sciences de Hongrie, Budapest, 1956.

Psychiatric Research Reports of the American Psychiatric Association: 3. Research in Psychosomatic Medicine. Edited by members of the Committee on Research, 1954-1955. Price, $2.00. Pp. 93. American Psychiatric Association, 1785 Massachusetts Ave., N. W., Washington 6, D. C., 1956.

Psychiatric Research Report of the American Psychitric Association: 4. An Evaluation of the Newer Psychopharmacologic Agents and Their Role in Current Psychiatric Practice. Edited by members of the Committee on Research, 1955-1956. Price, $2.00. Pp. 129. American Psychiatric Association, 1785 Massachusetts Ave., N. W., Washington 6, D. C., 1956.

BOOK REVIEWS

The Fields of Group Psychotherapy. Edited by S. R. Slavson. Price, $6.00. Pp. 338. International Universities Press, Inc., 227 W. 13th St., New York, 1956.

The reader opening "The Fields of Group Psychotherapy" might reasonably expect a book that outlines the areas in which group psychotherapy is effective, and perhaps something of an evaluation of this technique, especially as the editor is S. R. Slavson, whose name has been synonymous with this form of treatment for many years. The reader would be disap-

pointed. Instead of finding an integrated book, he will find a collection of papers of different theoretical orientations and practical interest. This is not to say that the volume is not valuable. On the contrary, its worth lies in its diversity and the contradictions in theory and practice which reflect the actual state of the field. The scope is broad and includes reports of psychoanalytic group psychotherapy, activity group therapy, directive group therapy, and what has been called "mass therapy," in which the group, by sheer weight of numbers, becomes unmanageable and, according to S. R. Slavson himself, not recognizable as clinical therapy.

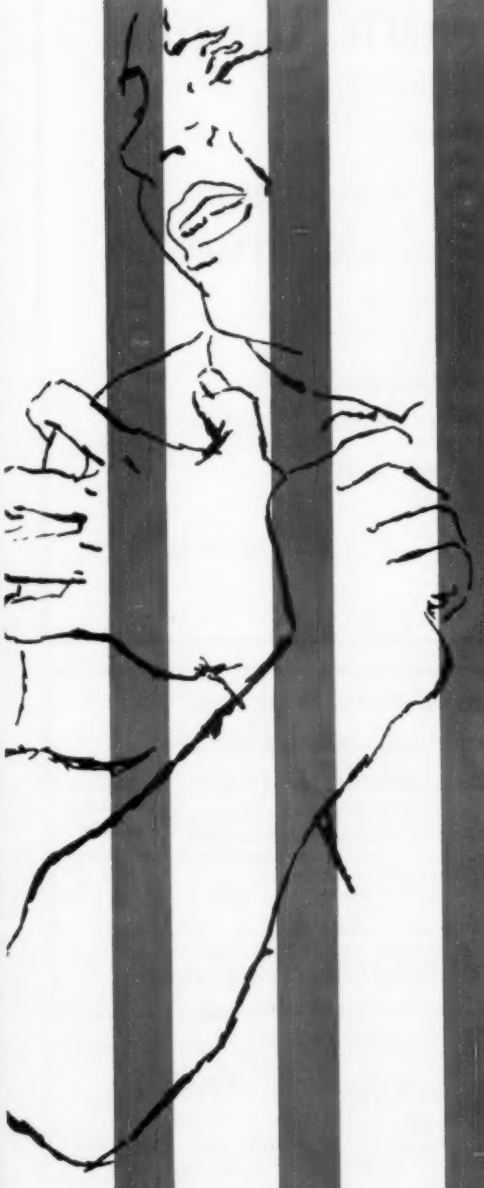
There are nineteen chapters, which cover the entire field of social and psychopathology, from the dynamics and treatment of behavior disorders of children to geriatrics. Each chapter is written by a therapist who has worked in the area, and contains a description of the field, a review of the literature, and a summary of actual group sessions with an attempt at evaluation of results of treatment. There are chapters on alcoholism, addiction, unwed mothers, private practice, and psychosomatic disorders, and, for an inexplicable reason, a separate one on allergies.

S. R. Slavson makes a valiant attempt at the outset to limit the field of study and to give a theoretical orientation for group psychotherapy. He emphasizes that grouping should be on the basis of similarity of pathology in terms of "nuclear problem." Such a group would, he reasons, enhance empathy and eventually insight. The group will respond "as though it was a single patient" and "in effect becomes one patient which makes possible treatment through the group." It is Slavson's contention that group psychotherapy can handle the less profound illnesses, while individual therapy and/or psychoanalysis is suitable for severe sexual trauma, prolonged anxiety states, and paralyzing ties to important persons, which, he feels, "require libidinal transference, therapeutic regression, and emerging insight." Each point is challenged in practice. T. R. Rees reports the grouping of psychotic patients at the Warlingham Park Hospital on the basis of symptoms such as soiling, degree of agitation, etc. Wilfred Hulse presents the case for mixed syndromes, and Hyman Miller and Dorothy Baruch treat allergic children who have pathological relationships with their parents by this technique.

Some of the more engaging studies are James Thorpe's original work on addiction, which includes the description of an outpatient clinic in Harlem for addicts, an excellent review of the literature of psychosomatic medicine, and the description of group therapy with peptic ulcer patients by Aaron Stein. T. R. Rees presents an inspiring, though remarkably undynamic, picture of the treatment center in England which he heads. The most successful studies, such as those on industry, teaching of medical students, the stutterers, have obvious goals and stress the role of the group leader. The least satisfactory chapters are on treatment of mothers, which is overly analytical, and that on sex and marriage, which represents the inspirational didactic group.

Benjamin Kotkov discusses the lack of research in group psychotherapy by emphasizing the enormous problems of quantification in therapy. Certainly the book bears out this statement. What is even more discouraging than the lack of research and some of the naïve criteria of improvement that the various investigators report is the absence of any substantial use made of the group dynamic technique to gather further data. The most consistent theory is borrowed completely from psychoanalysis and treats the group as an individual. Others, while stressing the social setting in which the individual manifests his symptoms, do not seem to utilize the group situation to explore this relationship. What is lacking is the use of group therapy to increase our knowledge of groups and thereby the problems inherent in socialization. Until this occurs, group psychotherapy must remain an applied psychiatry rather than a tool in basic research.

This book is recommended to those who want an overview of the practice of group techniques, and for those who want to know what has been accomplished with group psychotherapy in a specific area.



In Withdrawal Syndromes

Alcoholism

Drug addiction

As an agent to calm the acutely agitated, SPARINE has brought decisive relief to many hundreds of patients suffering from severe withdrawal symptoms.† SPARINE is rapidly effective by intravenous administration; maintenance is by the oral or intramuscular route.

In postalcoholic states, SPARINE offers prompt and marked remission of delirium tremens, acute hallucinosis, and tremulousness.†

In drug-addiction withdrawal, it promotes comfort by controlling nausea and vomiting and by inducing a view of detachment toward muscle and bone pains, abdominal cramps, and the general malaise.†

SPARINE is also effective in the management of acutely agitated psychotic patients. It tranquilizes them, making them more easily controlled and accessible to psychotherapy.†

†References on request.

NEW Potent Ataractic Drug

Sparine*

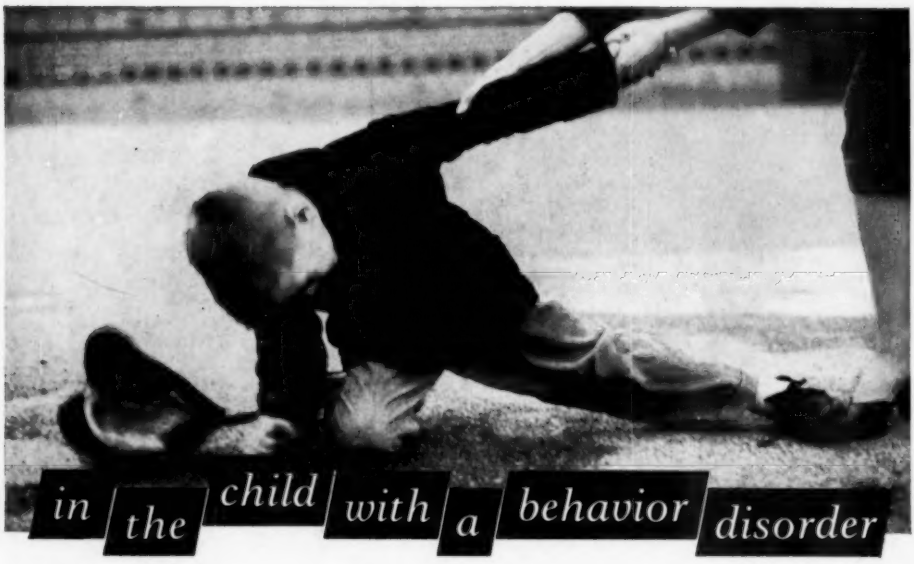
Promazine Hydrochloride — Hydrochloride

10-(γ-dimethylamino-*n*-propyl)-phenothiazine hydrochloride

*Trademark

Wyeth®

Philadelphia 1, Pa.



THORAZINE*

reduces hyperactivity and aggressiveness

decreases anxiety and hostility

improves mood, behavior and sleeping habits

establishes accessibility to guidance or psychotherapy

increases amenability to supervision

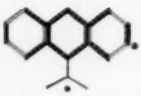
FACTS TO BEAR IN MIND

Even though the dramatic calming effect of 'Thorazine' on belligerent, overactive children may give the impression of a cure, simultaneous supportive counseling and guidance are necessary if lasting benefits are to be assured.

Adequate 'Thorazine' dosage for certain seriously disturbed youngsters will sometimes exceed 50-100 mg. t.i.d.

'Thorazine' should be administered discriminately and, before prescribing, the physician should be fully conversant with the available literature.

'Thorazine' is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).



Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.